



Lilly to Present Final Overall Survival Analysis from the MONARCH 3 Study of Verzenio® (abemaciclib) and Additional Results from Its Breast Cancer Portfolio at the 2023 San Antonio Breast Cancer Symposium

December 5, 2023

Results from MONARCH 3 show a numerical improvement in overall survival (OS) of 13.1 months for women with HR+, HER2- metastatic breast cancer treated with Verzenio plus an aromatase inhibitor in the intent-to-treat population and 14.9 months for women with visceral disease, however OS outcomes were not statistically significant

Additional analyses of Verzenio in metastatic and early breast cancer, as well as imlunestrant (oral SERD) in combination with Verzenio, will be presented at the meeting

INDIANAPOLIS, Dec. 5, 2023 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced results from the MONARCH 3 clinical trial, which will be presented in a late-breaking presentation during the 2023 San Antonio Breast Cancer Symposium (SABCS). MONARCH 3 evaluated Verzenio® (abemaciclib) in combination with an aromatase inhibitor (AI) compared to an AI alone as initial endocrine-based therapy for post-menopausal patients with hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) advanced or metastatic breast cancer. At eight years of follow-up, MONARCH 3 showed women taking Verzenio and an AI had a median overall survival (OS) of more than 5.5 years – an increase of 13.1 months compared to the control arm in the intent-to-treat (ITT) population (66.8 vs 53.7 months), although statistical significance for the OS outcome was not reached (HR, 0.804; 95% CI, 0.637-1.015; p=0.0664).

For women with visceral organ metastases, data showed a median OS of more than five years, with an increase in median OS of 14.9 months in the Verzenio arm compared to the control arm (63.7 vs 48.8 months). This included those women whose breast cancer has spread to the liver or lungs. Patients with visceral disease are at an increased risk of disease progression and death compared to metastatic breast cancer (MBC) patients without visceral metastases. The OS results for this subpopulation were also not statistically significant (HR, 0.758; 95% CI, 0.558-1.030; p=0.0757).

"At eight years of follow-up, when the natural history of metastatic breast cancer starts to substantially impact patient survival, it is highly encouraging to see abemaciclib combined with AI therapy deliver a meaningful survival difference of 13 months in the ITT population and more than 14 months in women at even higher risk due to visceral disease," said Stephen Johnston M.D., Ph.D., Professor of Breast Cancer Medicine and Consultant Medical Oncologist at The Royal Marsden NHS Foundation Trust (London, U.K.) and investigator on the MONARCH 3 trial. "Despite missing statistical significance, these data are clinically relevant and highly consistent with the overall body of evidence for abemaciclib in advanced or metastatic breast cancer."

The median progression free survival (PFS) benefit, the primary endpoint of the MONARCH 3 study, was maintained (29.0 vs 14.8 months; HR, 0.535; 95% CI, 0.429-0.668; nominal p<0.0001), with substantial difference in 6-year PFS rates (23.3% in the Verzenio arm vs 4.3% in the control arm). PFS statistical significance was achieved in an interim analysis in 2017, leading to global regulatory approvals for this indication in 2018. No new safety signals were observed with longer-term use.

"With a median OS of more than 5.5 years in patients treated with Verzenio in this study, these data further support the role of Verzenio in the survival of women with HR+, HER2- metastatic breast cancer," said David Hyman, M.D., chief medical officer, Lilly. "We remain confident in the differentiated profile of Verzenio and we look forward to sharing these results with the clinical community at SABCS and getting their perspective on these data and relevance for clinical practice."

The full results will be shared in a late-breaking presentation on Wednesday, December 6, 11:45 a.m. – 12:00 p.m. CST in General Session 1, Hall 1.

Additional Verzenio data will be presented at SABCS. In early breast cancer (EBC), an oral presentation will provide results from genomic and transcriptomic profiling analyses of archived primary tumor tissue from patients with HR+, HER2-, node-positive, high risk EBC in the monarchE trial and associate it with the study's ITT clinical outcomes. A poster spotlight discussion will show results from a pilot study exploring ctDNA detection using a tumor-informed assay in the monarchE trial to identify patients at high risk of recurrence. Other planned Verzenio disclosures in both MBC and EBC are listed in the table below.

Imlunestrant (investigational oral SERD)

Updated results from the EMBER study of imlunestrant monotherapy as well as imlunestrant in combination with Verzenio, with or without an AI, in patients with estrogen receptor positive (ER+), HER2- advanced breast cancer will be presented in a spotlight poster discussion. With 5.5 months longer follow-up from the last disclosure, imlunestrant plus Verzenio with or without an AI resulted in an ORR of 62% and 32%, respectively, and a clinical benefit rate (CBR) of 79% and 71%, respectively. CBR is the percentage of patients with advanced or metastatic cancer who have achieved complete response, partial response and prolonged stable disease for 24 weeks or more. The most common TEAEs for patients treated with imlunestrant plus Verzenio were diarrhea, nausea, fatigue, and neutropenia. No safety signals related to ocular or cardiac toxicity were observed. Side effects from imlunestrant were generally low grade and there were few dose reductions or discontinuations of imlunestrant.

A full list of abstract titles and viewing details are listed below:

Medicine	Abstract Title	Presentation Details
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Verzenio (abemaciclib)	MONARCH 3: Final overall survival results of abemaciclib plus a nonsteroidal aromatase inhibitor as first-line therapy in patients with HR+, HER2- advanced breast cancer	Abstract #: 1643629 Presentation ID: GS01-12 Session Type: Late Breaking Oral Date & Time: Wednesday, December 6, 11:45 a.m. – 12:00 p.m. CST Presenter: M Goetz
Verzenio (abemaciclib)	Genomic and transcriptomic profiling of primary tumors from patients with HR+, HER2-, node-positive, high-risk early breast cancer in the monarchE trial	Abstract #: 1569529 Poster ID: GS03-06 Session Type: Oral Date & Time: Friday, December 8, 9:35 – 9:45 a.m. CST Presenter: N Turner
Verzenio (abemaciclib)	Results from a pilot study exploring ctDNA detection using a tumor-informed assay in the monarchE trial of adjuvant abemaciclib with endocrine therapy in HR+, HER2-, node-positive, high-risk early breast cancer	Abstract #: 1580352 Poster ID: PS06-01 Session Type: Poster Spotlight Discussion Date & Time: Wednesday, December 6, 7:00 – 7:04 a.m. CST Presenter: S Graff
Verzenio (abemaciclib)	Safety profiles of Chinese breast cancer patients who received abemaciclib in MONARCH plus and monarchE study	Abstract #: 1575371 Poster ID: PO1-13-01 Session Type: Poster Session 1 Date & Time: Wednesday, December 6, 12:00 – 2:00 p.m. CST Presenter: Z Jiang
Verzenio (abemaciclib)	Real-world clinical outcomes in US patients with brain metastases secondary to HR+/HER2- metastatic breast cancer treated with abemaciclib	Abstract #: 1577336 Poster ID: PO1-17-01 Session Type: Poster Session 1 Date & Time: Wednesday, December 6, 12:00 – 2:00 p.m. CST Presenter: W Mwangi
Verzenio (abemaciclib)	Circulating tumor DNA mutation landscape in HR+/HER2- patients with mBC treated with cyclin-dependent kinase 4/6 inhibitors in the SCRUM-Japan MONSTAR-SCREEN study	Abstract #: 1549969 Poster ID: PO1-13-02 Session Type: Poster Session 1 Date & Time: Wednesday, December 6, 12:00 – 2:00 p.m. CST Presenter: M Hattori
Imlunestrant	Imlunestrant monotherapy and in combination with abemaciclib, with or without an aromatase inhibitor, in estrogen receptor-positive (ER+), HER2-negative (HER2-) advanced breast cancer (aBC): updated results from the EMBER study	Abstract #: 1545518 Poster ID: PS15-09 Session Type: Poster Spotlight Discussion Date & Time: Thursday, December 7, 6:12 – 6:16 p.m. CST Presenter: KL Jhaveri

About the MONARCH 3 Study

[MONARCH 3](#) was a Phase 3, double-blind, placebo-controlled study designed to evaluate the safety and efficacy of Verzenio in combination with an aromatase inhibitor (AI) (anastrozole or letrozole), as initial endocrine-based therapy for postmenopausal women with HR+, HER2- advanced (locoregionally recurrent or metastatic) breast cancer who have had no prior systemic treatment for advanced disease. If neoadjuvant/adjuvant endocrine therapy was administered, a disease-free interval of more than 12 months since completion of endocrine therapy was required. A total of 493 patients were randomized 2:1 to receive 150 mg of Verzenio or placebo orally twice a day, without interruption, given in combination with either 1 mg of anastrozole or 2.5 mg of letrozole once daily until disease progression or unacceptable toxicity. The primary endpoint of the study was progression-free survival (PFS) and secondary endpoints include overall survival (OS), overall response rate (ORR), duration of response (DoR), and safety. OS is the only alpha-controlled secondary outcome measure, and this analysis is split among two populations (intent-to-treat [ITT] and the subgroup with visceral disease).

About Metastatic Breast Cancer

Advanced breast cancer includes metastatic breast cancer, meaning cancer that has spread from the breast tissue to other parts of the body, and locally or regionally advanced breast cancer, meaning the cancer has grown outside the organ where it started but has not yet spread to other parts of the body.¹ Of all early-stage breast cancer cases diagnosed in the U.S., approximately 30% will become metastatic² and an estimated 6-10% of all new breast cancer cases are initially diagnosed as being metastatic.³ Survival is lower among women with a more advanced stage of disease at diagnosis: five-year relative survival is 99% for localized disease, 86% for regional disease, and 30% for metastatic disease.⁴ Other factors, such as tumor size, also impact five-year survival estimates.⁴

About Breast Cancer

Breast cancer has surpassed lung cancer as the most commonly diagnosed cancer worldwide, according to GLOBOCAN. The estimated 2.3 million new cases indicate that 1 in every 8 cancers diagnosed in 2020 is breast cancer. With approximately 685,000 deaths in 2020, breast cancer is the fifth-leading cause of cancer death worldwide.⁵ In the U.S., it is estimated that there will be more than 300,000 new cases of breast cancer diagnosed in 2023. Breast cancer is the second leading cause of cancer death in women in the U.S.⁶

About Verzenio® (abemaciclib)

Verzenio® (abemaciclib) is approved to treat people with certain HR+, HER2- breast cancers in the adjuvant and advanced or metastatic setting. Verzenio is the first and only CDK4/6 inhibitor approved to treat node-positive, high risk early breast cancer (EBC) patients.⁷ For HR+, HER2- breast cancer, The National Comprehensive Cancer Network® (NCCN®) recommends consideration of two years of abemaciclib (Verzenio) added to endocrine therapy as a Category 1 treatment option in the adjuvant setting.⁸ NCCN® also includes Verzenio plus endocrine therapy as a preferred treatment option for HR+, HER2- metastatic breast cancer.⁸

The collective results of Lilly's clinical development program continue to differentiate Verzenio as a CDK4/6 inhibitor. In HR+, HER2-, high risk EBC, Verzenio has shown a persistent and deepening benefit beyond the two-year treatment period in the monarchE trial, the only adjuvant study designed to investigate a CDK4/6 inhibitor specifically in a node-positive, high risk EBC population.⁹ In HR+, HER2-, metastatic breast cancer, Verzenio has demonstrated statistically significant overall survival in the Phase 3 MONARCH 2 study.¹⁰ Verzenio has shown a consistent and generally manageable safety profile across clinical trials. In addition to breast cancer, Lilly is studying Verzenio in different forms of difficult-to-treat prostate cancer.

Verzenio is an oral tablet taken twice daily and available in strengths of 50 mg, 100 mg, 150 mg, and 200 mg. Discovered and developed by Lilly researchers, Verzenio was first approved in 2017 and is currently authorized for use in more than 90 countries around the world. For full details on indicated uses of Verzenio in HR+, HER2- breast cancer, please see full [Prescribing Information](#), available at www.Verzenio.com.

INDICATIONS FOR VERZENIO®

VERZENIO® is a kinase inhibitor indicated:

- in combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence.
- in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.
- in combination with fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.
- as monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.

IMPORTANT SAFETY INFORMATION FOR VERZENIO (abemaciclib)

Severe **diarrhea** associated with dehydration and infection occurred in patients treated with Verzenio. Across four clinical trials in 3691 patients, diarrhea occurred in 81 to 90% of patients who received Verzenio. Grade 3 diarrhea occurred in 8 to 20% of patients receiving Verzenio. Most patients experienced diarrhea during the first month of Verzenio treatment. The median time to onset of the first diarrhea event ranged from 6 to 8 days; and the median duration of Grade 2 and Grade 3 diarrhea ranged from 6 to 11 days and 5 to 8 days, respectively. Across trials, 19 to 26% of patients with diarrhea required a Verzenio dose interruption and 13 to 23% required a dose reduction.

Instruct patients to start antidiarrheal therapy, such as loperamide, at the first sign of loose stools, increase oral fluids, and notify their healthcare provider for further instructions and appropriate follow-up. For Grade 3 or 4 diarrhea, or diarrhea that requires hospitalization, discontinue Verzenio until toxicity resolves to ≤Grade 1, and then resume Verzenio at the next lower dose.

Neutropenia, including febrile neutropenia and fatal neutropenic sepsis, occurred in patients treated with Verzenio. Across four clinical trials in 3691 patients, neutropenia occurred in 37 to 46% of patients receiving Verzenio. A Grade ≥3 decrease in neutrophil count (based on laboratory findings) occurred in 19 to 32% of patients receiving Verzenio. Across trials, the median time to first episode of Grade ≥3 neutropenia ranged from 29 to 33 days, and the median duration of Grade ≥3 neutropenia ranged from 11 to 16 days. Febrile neutropenia has been reported in <1% of patients exposed to Verzenio across trials. Two deaths due to neutropenic sepsis were observed in MONARCH 2. Inform patients to promptly report any episodes of fever to their healthcare provider.

Monitor complete blood counts prior to the start of Verzenio therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia.

Severe, life-threatening, or fatal **interstitial lung disease (ILD) or pneumonitis** can occur in patients treated with Verzenio and other CDK4/6 inhibitors. In Verzenio-treated patients in EBC (monarchE), 3% of patients experienced ILD or pneumonitis of any grade: 0.4% were Grade 3 or 4 and there was one fatality (0.1%). In Verzenio-treated patients in MBC (MONARCH 1, MONARCH 2, MONARCH 3), 3.3% of Verzenio-treated patients had ILD or pneumonitis of any grade: 0.6% had Grade 3 or 4, and 0.4% had fatal outcomes. Additional cases of ILD or pneumonitis have been observed in the postmarketing setting, with fatalities reported.

Monitor patients for pulmonary symptoms indicative of ILD or pneumonitis. Symptoms may include hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic exams. Infectious, neoplastic, and other causes for such symptoms should be excluded by means of appropriate investigations. Dose interruption or dose reduction is recommended in patients who develop persistent or recurrent Grade 2 ILD or pneumonitis. Permanently discontinue Verzenio in all patients with Grade 3 or 4 ILD or pneumonitis.

Grade ≥3 increases in alanine aminotransferase (ALT) (2 to 6%) and **aspartate aminotransferase (AST)** (2 to 3%) were reported in patients receiving Verzenio. Across three clinical trials in 3559 patients (monarchE, MONARCH 2, MONARCH 3), the median time to onset of Grade ≥3 ALT increases ranged from 57 to 87 days and the median time to resolution to Grade <3 was 13 to 14 days. The median time to onset of Grade ≥3 AST increases ranged from 71 to 185 days and the median time to resolution to Grade <3 ranged from 11 to 15 days.

Monitor liver function tests (LFTs) prior to the start of Verzenio therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Dose interruption, dose reduction, dose discontinuation, or delay in starting treatment cycles is recommended for patients who develop persistent or recurrent Grade 2, or any Grade 3 or 4 hepatic transaminase elevation.

Venous thromboembolic events (VTE) were reported in 2 to 5% of patients across three clinical trials in 3559 patients treated with Verzenio (monarchE, MONARCH 2, MONARCH 3). VTE included deep vein thrombosis, pulmonary embolism, pelvic venous thrombosis, cerebral venous sinus thrombosis, subclavian and axillary vein thrombosis, and inferior vena cava thrombosis. In clinical trials, deaths due to VTE have been reported in patients treated with Verzenio.

Verzenio has not been studied in patients with early breast cancer who had a history of VTE. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate. Dose interruption is recommended for EBC patients with any grade VTE and for MBC patients with a Grade 3 or 4 VTE.

Verzenio can cause **fetal harm** when administered to a pregnant woman, based on findings from animal studies and the mechanism of action. In animal reproduction studies, administration of abemaciclib to pregnant rats during the period of organogenesis caused teratogenicity and decreased fetal weight at maternal exposures that were similar to the human clinical exposure based on area under the curve (AUC) at the maximum recommended human dose. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Verzenio and for 3 weeks after the last dose. Based on findings in animals, Verzenio may impair fertility in males of reproductive potential. There are no data on the presence of Verzenio in human milk or its effects on the breastfed child or on milk production. Advise lactating women not to breastfeed during Verzenio treatment and for at least 3 weeks after the last dose because of the potential for serious adverse reactions in breastfed infants.

The **most common adverse reactions (all grades, $\geq 10\%$)** observed in **monarchE for Verzenio plus tamoxifen or an aromatase inhibitor vs tamoxifen or an aromatase inhibitor, with a difference between arms of $\geq 2\%$** , were diarrhea (84% vs 9%), infections (51% vs 39%), neutropenia (46% vs 6%), fatigue (41% vs 18%), leukopenia (38% vs 7%), nausea (30% vs 9%), anemia (24% vs 4%), headache (20% vs 15%), vomiting (18% vs 4.6%), stomatitis (14% vs 5%), lymphopenia (14% vs 3%), thrombocytopenia (13% vs 2%), decreased appetite (12% vs 2.4%), ALT increased (12% vs 6%), AST increased (12% vs 5%), dizziness (11% vs 7%), rash (11% vs 4.5%), and alopecia (11% vs 2.7 %).

The **most frequently reported $\geq 5\%$ Grade 3 or 4 adverse reaction** that occurred in the Verzenio arm vs the tamoxifen or an aromatase inhibitor arm of monarchE were neutropenia (19.6% vs 1%), leukopenia (11% vs <1%), diarrhea (8% vs 0.2%), and lymphopenia (5% vs <1%).

Lab abnormalities (all grades; Grade 3 or 4) for **monarchE in $\geq 10\%$ for Verzenio plus tamoxifen or an aromatase inhibitor with a difference between arms of $\geq 2\%$** were increased serum creatinine (99% vs 91%; .5% vs <.1%), decreased white blood cells (89% vs 28%; 19.1% vs 1.1%), decreased neutrophil count (84% vs 23%; 18.7% vs 1.9%), anemia (68% vs 17%; 1% vs .1%), decreased lymphocyte count (59% vs 24%; 13.2 % vs 2.5%), decreased platelet count (37% vs 10%; .9% vs .2%), increased ALT (37% vs 24%; 2.6% vs 1.2%), increased AST (31% vs 18%; 1.6% vs .9%), and hypokalemia (11% vs 3.8%; 1.3% vs 0.2%).

The **most common adverse reactions (all grades, $\geq 10\%$)** observed in **MONARCH 3 for Verzenio plus anastrozole or letrozole vs anastrozole or letrozole, with a difference between arms of $\geq 2\%$** , were diarrhea (81% vs 30%), fatigue (40% vs 32%), neutropenia (41% vs 2%), infections (39% vs 29%), nausea (39% vs 20%), abdominal pain (29% vs 12%), vomiting (28% vs 12%), anemia (28% vs 5%), alopecia (27% vs 11%), decreased appetite (24% vs 9%), leukopenia (21% vs 2%), creatinine increased (19% vs 4%), constipation (16% vs 12%), ALT increased (16% vs 7%), AST increased (15% vs 7%), rash (14% vs 5%), pruritus (13% vs 9%), cough (13% vs 9%), dyspnea (12% vs 6%), dizziness (11% vs 9%), weight decreased (10% vs 3.1%), influenza-like illness (10% vs 8%), and thrombocytopenia (10% vs 2%).

The **most frequently reported $\geq 5\%$ Grade 3 or 4 adverse reactions** that occurred in the Verzenio arm vs the placebo arm of **MONARCH 3** were neutropenia (22% vs 1%), diarrhea (9% vs 1.2%), leukopenia (7% vs <1%), increased ALT (6% vs 2%), and anemia (6% vs 1%).

Lab abnormalities (all grades; Grade 3 or 4) for **MONARCH 3 in $\geq 10\%$ for Verzenio plus anastrozole or letrozole with a difference between arms of $\geq 2\%$** were increased serum creatinine (98% vs 84%; 2.2% vs 0%), decreased white blood cells (82% vs 27%; 13% vs 0.6%), anemia (82% vs 28%; 1.6% vs 0%), decreased neutrophil count (80% vs 21%; 21.9% vs 2.6%), decreased lymphocyte count (53% vs 26%; 7.6% vs 1.9%), decreased platelet count (36% vs 12%; 1.9% vs 0.6%), increased ALT (48% vs 25%; 6.6% vs 1.9%), and increased AST (37% vs 23%; 3.8% vs 0.6%).

The **most common adverse reactions (all grades, $\geq 10\%$)** observed in **MONARCH 2 for Verzenio plus fulvestrant vs fulvestrant, with a difference between arms of $\geq 2\%$** , were diarrhea (86% vs 25%), neutropenia (46% vs 4%), fatigue (46% vs 32%), nausea (45% vs 23%), infections (43% vs 25%), abdominal pain (35% vs 16%), anemia (29% vs 4%), leukopenia (28% vs 2%), decreased appetite (27% vs 12%), vomiting (26% vs 10%), headache (20% vs 15%), dysgeusia (18% vs 2.7%), thrombocytopenia (16% vs 3%), alopecia (16% vs 1.8%), stomatitis (15% vs 10%), ALT increased (13% vs 5%), pruritus (13% vs 6%), cough (13% vs 11%), dizziness (12% vs 6%), AST increased (12% vs 7%), peripheral edema (12% vs 7%), creatinine increased (12% vs <1%), rash (11% vs 4.5%), pyrexia (11% vs 6%), and weight decreased (10% vs 2.2%).

The **most frequently reported $\geq 5\%$ Grade 3 or 4 adverse reactions** that occurred in the Verzenio arm vs the placebo arm of **MONARCH 2** were neutropenia (25% vs 1%), diarrhea (13% vs 0.4%), leukopenia (9% vs 0%), anemia (7% vs 1%), and infections (5.7% vs 3.5%).

Lab abnormalities (all grades; Grade 3 or 4) for **MONARCH 2 in $\geq 10\%$ for Verzenio plus fulvestrant with a difference between arms of $\geq 2\%$** were increased serum creatinine (98% vs 74%; 1.2% vs 0%), decreased white blood cells (90% vs 33%; 23.7% vs .9%), decreased neutrophil count (87% vs 30%; 32.5% vs 4.2%), anemia (84% vs 34%; 2.6% vs .5%), decreased lymphocyte count (63% vs 32%; 12.2% vs 1.8%), decreased platelet count (53% vs 15%; 2.1% vs 0%), increased ALT (41% vs 32%; 4.6% vs 1.4%), and increased AST (37% vs 25%; 3.9% vs 4.2%).

The **most common adverse reactions (all grades, $\geq 10\%$)** observed in **MONARCH 1** with Verzenio were diarrhea (90%), fatigue (65%), nausea (64%), decreased appetite (45%), abdominal pain (39%), neutropenia (37%), vomiting (35%), infections (31%), anemia (25%), thrombocytopenia (20%), headache (20%), cough (19%), constipation (17%), leukopenia (17%), arthralgia (15%), dry mouth (14%), weight decreased (14%), stomatitis (14%), creatinine increased (13%), alopecia (12%), dysgeusia (12%), pyrexia (11%), dizziness (11%), and dehydration (10%).

The **most frequently reported $\geq 5\%$ Grade 3 or 4 adverse reactions** from **MONARCH 1** with Verzenio were diarrhea (20%), neutropenia (24%), fatigue (13%), and leukopenia (5%).

Lab abnormalities (all grades; Grade 3 or 4) for MONARCH 1 with Verzenio were increased serum creatinine (99%; .8%), decreased white blood cells (91%; 28%), decreased neutrophil count (88%; 26.6%), anemia (69%; 0%), decreased lymphocyte count (42%; 13.8%), decreased platelet count (41%; 2.3%), increased ALT (31%; 3.1%), and increased AST (30%; 3.8%).

Strong and moderate CYP3A inhibitors increased the exposure of abemaciclib plus its active metabolites to a clinically meaningful extent and may lead to increased toxicity. Avoid concomitant use of ketoconazole. Ketoconazole is predicted to increase the AUC of abemaciclib by up to 16-fold. In patients with recommended starting doses of 200 mg twice daily or 150 mg twice daily, reduce the Verzenio dose to 100 mg twice daily with concomitant use of strong CYP3A inhibitors other than ketoconazole. In patients who have had a dose reduction to 100 mg twice daily due to adverse reactions, further reduce the Verzenio dose to 50 mg twice daily with concomitant use of strong CYP3A inhibitors. If a patient taking Verzenio discontinues a strong CYP3A inhibitor, increase the Verzenio dose (after 3 to 5 half-lives of the inhibitor) to the dose that was used before starting the inhibitor. With concomitant use of moderate CYP3A inhibitors, monitor for adverse reactions and consider reducing the Verzenio dose in 50 mg decrements. Patients should avoid grapefruit products.

Avoid concomitant use of strong or moderate CYP3A inducers and consider alternative agents. Coadministration of strong or moderate CYP3A inducers decreased the plasma concentrations of abemaciclib plus its active metabolites and may lead to reduced activity.

With severe hepatic impairment (Child-Pugh C), reduce the Verzenio dosing frequency to once daily. The pharmacokinetics of Verzenio in patients with **severe renal impairment** (CL_{cr} <30 mL/min), end stage renal disease, or in patients on dialysis is unknown. No dosage adjustments are necessary in patients with mild or moderate hepatic (Child-Pugh A or B) and/or renal impairment (CL_{cr} ≥30-89 mL/min).

Please see full [Prescribing Information](#) and [Patient Information](#) for Verzenio.

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About the EMBER Study

This global, first-in-human, open-label Phase 1a/b trial evaluates imlunestrant alone or in combination with other anticancer therapies in participants with ER+ advanced breast cancer or endometrioid endometrial cancer. The trial includes a Phase 1a dose escalation phase and a Phase 1b dose expansion phase. The Phase 1a dose escalation enrolls patients with ER+, HER2- advanced breast cancer who have received up to three prior treatment regimens and ER+ EEC who have progressed after prior platinum-based therapy. The dose escalation phase followed an i3+3 design with imlunestrant administered orally in 28-day cycles. As dose cohorts were cleared, additional patient enrollment to cleared dose levels was permitted. The primary objective of the Phase 1a portion is to determine the recommended Phase 2 dose. Secondary objectives include assessments of safety, pharmacokinetics, and anti-tumor activity (objective response rate [ORR] and clinical benefit rate [CBR], as assessed per Response Evaluation Criteria in Solid Tumors [RECIST v1.1]).

About Imlunestrant

Imlunestrant (LY3484356) is an investigational, next-generation oral selective estrogen receptor degrader (SERD) with pure antagonistic properties. The estrogen receptor (ER) is the key therapeutic target for patients with ER+/HER2- breast cancer. Novel degraders of ER may overcome endocrine therapy resistance while providing consistent oral pharmacology and convenience of administration. Imlunestrant was specifically designed to deliver continuous estrogen receptor target inhibition throughout the dosing period and regardless of ESR1 mutational status. Imlunestrant is currently being studied in several clinical studies.

About Lilly

Lilly unites caring with discovery to create medicines that make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 51 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges, redefining diabetes care, treating obesity and curtailing its most devastating long-term effects, advancing the fight against Alzheimer's disease, providing solutions to some of the most debilitating immune system disorders, and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit [Lilly.com](https://www.lilly.com) and [Lilly.com/news](https://www.lilly.com/news) or follow us on [Facebook](https://www.facebook.com/lilly), [Instagram](https://www.instagram.com/lilly) and [LinkedIn](https://www.linkedin.com/company/lilly). P-LLY

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NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Verzenio as a treatment for people with certain types of breast cancer and imlunestrant as a potential treatment for people with certain types of breast cancer and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, that Verzenio will receive additional regulatory approvals, or that imlunestrant will prove to be a safe and effective treatment for certain types of breast cancer or receive regulatory approval. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

¹ American Cancer Society. Understanding Advanced Cancer, Metastatic Cancer and Bone Metastases. <https://www.cancer.org/treatment/understanding-your-diagnosis/advanced-cancer/what-is.html>. Accessed November 30, 2023.

² O'Shaughnessy J. Extending survival with chemotherapy in metastatic breast cancer. *Oncologist*. 2005;10 Suppl 3:20-9. PMID: 16368868 DOI: 10.1634/theoncologist.10-90003-20.

³ Metastatic Breast Cancer Network. 13 Facts about Metastatic Breast Cancer. <http://www.mbcn.org/13-facts-about-metastatic-breast-cancer/>.

Accessed November 30, 2023.

⁴ American Cancer Society. Breast Cancer Facts & Figures 2022-2024. Atlanta: American Cancer Society, Inc. 2022. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/2022-2024-breast-cancer-fact-figures-acf.pdf>. Accessed November 30, 2023.

⁵ Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-249.

⁶ American Cancer Society. Cancer Statistics Center. <http://cancerstatisticscenter.cancer.org>. Accessed November 30, 2023.

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⁸ Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines[®]) for Breast Cancer V.4.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed October 18, 2023. To view the most recent and complete version of the guidelines, go online to [NCCN.org](https://www.nccn.org). NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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