

Name: Katherine Posther Sugarman, MD
Title: Vice President, Global Medical Affairs - Oncology
Company: Eli Lilly and Company
Address: Lilly Corporate Center, Indianapolis, IN 46285
Phone: 317-277-8213
Email: sugarmank@lilly.com
Date of Request: February 26, 2018
NCCN Guideline Panel: Breast Cancer

On behalf of Eli Lilly and Company, I respectfully request the NCCN Breast Cancer Guideline Panel to review the enclosed data for consideration of inclusion of VERZENIO™ (abemaciclib) in combination with an aromatase inhibitor (AI) as an initial endocrine-based treatment option for postmenopausal women with hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) advanced or metastatic breast cancer (MBC) in the Breast Cancer Guideline.

- **Request for NCCN Guideline Panel to consider review of data for a specific indication:**
 - The MONARCH 3 trial studied abemaciclib in combination with an AI in postmenopausal women with HR+, HER2- advanced or MBC with no prior systemic therapy in this disease setting. The median progression-free survival (PFS) was 28.2 months (95% CI: 23.5, not reached) for abemaciclib plus AI and 14.8 months (95% CI: 11.2, 19.2) for placebo plus AI (hazard ratio 0.540, 95% CI, 0.418–0.698, p<.0001).
- **Specific changes recommended within the NCCN Guideline:**
 - The recommended change is to update the NCCN Guideline to add the combination of abemaciclib with an AI as an initial endocrine-based treatment option for postmenopausal women with HR+, HER2- advanced or MBC.
- **Statement of FDA approval status:**
 - The submitted use was approved by the US Food and Drug Administration (FDA) on February 26, 2018.¹
- **Rationale for recommended change:**
 - On February 26, 2018, the FDA approved abemaciclib for use in combination with an AI as initial endocrine-based therapy for the treatment of postmenopausal women with HR+, HER2- advanced or MBC.¹ Please see prescribing information for approved label information.
- **Citation of literature support and complete articles supporting recommended change:**
 - FDA Approval Letter
 - [VERZENIO™ \(abemaciclib\) Prescribing Information](#)
 - [Goetz MP, Toi M, Campone M, et al. MONARCH 3: Abemaciclib as initial therapy for advanced breast cancer. *J Clin Oncol*. 2017;35\(32\):3638-3646.](#)

[MONARCH 3](#) was a randomized (2:1), double-blinded, placebo-controlled, multicenter phase 3 study of abemaciclib or placebo with an AI (anastrozole or letrozole) in postmenopausal women with HR+, HER2- advanced or MBC with no prior systemic therapy in this disease setting.^{2,3} Efficacy results from MONARCH 3 are summarized in Table 1. Progression-free survival was evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, and the PFS assessment based on a blinded independent radiologic review was consistent with the investigator assessment. Consistent results were observed across patient stratification subgroups of disease site and prior (neo)adjuvant endocrine therapy. At the time of PFS analysis, 19% of patients had died, and overall survival data were immature.²

Table 1. MONARCH 3 Efficacy Results (ITT Population, Investigator Assessment)²

	Abemaciclib + Anastrozole or Letrozole	Placebo + Anastrozole or Letrozole
Progression-free survival	N=328	N=165
Number of patients with an event, n (%)	138 (42.1)	108 (65.5)
Median, months (95% CI)	28.2 (23.5, NR)	14.8 (11.2, 19.2)
Hazard ratio (95% CI)	0.540 (0.418, 0.698)	
P value	<.0001	
Objective response for patients with measurable disease	N=267	N=132
Objective response rate ^{a,b} , n (%)	148 (55.4)	53 (40.2)
95% CI	49.5, 61.4	31.8, 48.5

Abbreviations: CI = confidence interval; ITT = intent-to-treat; NR = not reached.

^a Complete response + partial response.

^b Based on confirmed responses.

In the abemaciclib plus AI arm, the most common adverse reactions reported ($\geq 20\%$) of any grade included diarrhea, neutropenia, fatigue, infections, nausea, abdominal pain, anemia, vomiting, alopecia, decreased appetite, and leukopenia.² Diarrhea was predominately low grade, had a median onset of 8 days, and was managed by dose adjustment and antidiarrheal medication.^{2,3} Permanent discontinuation of abemaciclib therapy due to diarrhea was infrequent (2%). Neutropenia was observed in 41% of all patients in the abemaciclib plus AI arm, with grade ≥ 3 neutropenia reported in 22% of patients.² Febrile neutropenia was reported in one patient in the abemaciclib plus AI arm and was considered nonserious.³ Venous thromboembolic events (VTEs) occurred in 5% of patients in the abemaciclib plus AI arm and included deep vein thrombosis, pulmonary embolism, and pelvic venous thrombosis. Permanent discontinuation of abemaciclib therapy due to VTEs was infrequent (1%).²

MONARCH 3 demonstrated that abemaciclib in combination with an AI was a generally well-tolerated initial therapy which significantly improved PFS and objective response rate in patients with HR+, HER2- advanced or MBC.^{2,3} These data support consideration of abemaciclib in combination with an AI as an initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor HR+, HER2- advanced or MBC.

We appreciate the Panel's thorough consideration of Lilly's recommendation that abemaciclib in combination with an AI be added as an initial endocrine-based treatment option for postmenopausal women with HR+, HER2- advanced or MBC. Please do not hesitate to contact me with any questions.

Sincerely,

Katherine Posther Sugarman, MD
Vice President, Global Medical Affairs - Oncology
Eli Lilly and Company

References:

1. FDA Approval Letter

2. VERZENIO™ (abemaciclib) Prescribing Information

3. Goetz MP, et al. *J Clin Oncol.* 2017;35(32):3638-3646