Name: Lynn McRoy MD FACS
Company/Organization: Pfizer Inc. Oncology
Address: 235 East 42nd Street, MS 219-6, New York, New York 10017
Phone: 212-733-1511
Email: lynn.mcroy@pfizer.com
Date of request: April 26, 2016
NCCN Guidelines Panel: Breast Cancer

Dear Ms. McClure,

On behalf of Pfizer Oncology, I respectfully request the NCCN Breast Cancer Guideline Panel to review the enclosed for consideration of updating the NCCN Breast Cancer Guideline indicated use of IBRANCE® (palbociclib) in combination with fulvestrant as a treatment option in hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

Request for NCCN Guidelines Panel to consider review of data for a specific indication:

- IBRANCE (palbociclib) in combination with fulvestrant

- **Specific changes recommended within the NCCN Guidelines:**
  - Currently the NCCN guidelines state the combination may be appropriate for postmenopausal women or premenopausal women receiving ovarian suppression with an LHRH agonist with hormone receptor positive and HER2 negative metastatic breast cancer that has progressed on prior endocrine therapy.
  - Request the following change: for postmenopausal women or premenopausal women receiving ovarian suppression with an LHRH agonist with hormone receptor positive and HER2 negative metastatic breast cancer that has progressed *on or after prior adjuvant or metastatic endocrine therapy*

- **Statement of whether the submitted use is or is not FDA approved for that indication**
  - Approved on February 19, 2016
- **Rationale for recommended change**
  - The current wording in the NCCN guidelines may lead to the conclusion that to be eligible for treatment with IBRANCE in combination with Fulvestrant patients must have progressed *during* endocrine therapy. Third party payers may create clinical policies that restrict coverage to this subset of patients**.**

    The USPI for IIBRANCE states in Section14 Clinical Studies**:**

> **Study 2: IBRANCE plus Fulvestrant**
>
> Study 2 was an international, randomized, double-blind, parallel group, multicenter study of IBRANCE plus fulvestrant versus placebo plus fulvestrant conducted in women with HR-positive, HER2-negative advanced breast cancer, regardless of their menopausal status, ***whose disease progressed on or after prior endocrine therapy****[1]. A total of 521 pre/postmenopausal women were randomized 2:1 to IBRANCE plus fulvestrant or placebo plus fulvestrant and stratified by documented sensitivity to prior hormonal therapy, menopausal status at study entry (pre/peri versus postmenopausal), and presence of visceral

[1] Italics added

metastases. IBRANCE was given orally at a dose of 125 mg daily for 21 consecutive days followed by 7 days off treatment. Pre/perimenopausal women were enrolled in the study and received the LHRH agonist goserelin for at least 4 weeks prior to and for the duration of Study 2. Patients continued to receive assigned treatment until objective disease progression, symptomatic deterioration, unacceptable toxicity, death, or withdrawal of consent, whichever occurred first. The major efficacy outcome of the study was investigator-assessed PFS evaluated according to RECIST 1.1.

Patients enrolled in this study had a median age of 57 years (range 29 to 88). The majority of patients on study were White (74%), all patients had an ECOG PS of 0 or 1, and 80% were postmenopausal. All patients had received prior systemic therapy and 75% of patients had received a previous chemotherapy regimen. Twenty-five percent of patients had received no prior therapy in the metastatic disease setting, 60% had visceral metastases, and 23% had bone only disease.[1]

The enrollment eligibility for study 2 (Paloma 3) states:
"Disease relapse or progression had to occur after previous endocrine therapy (with an aromatase inhibitor if the patient was postmenopausal or with tamoxifen if premenopausal or perimenopausal) while on or within 1 month after treatment in the advanced setting, or while on or within 12 months of completion of adjuvant therapy irrespective of menopausal status. One previous line of chemotherapy in advanced disease was allowed".[2]

- **Citation of literature support and complete articles supporting recommended change (attached):**

USPI - Ibrance - palbociclib - capsules

  - **1.** USPI
  - **2.** Cristofanilli, Turner, et al**.** Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): final analysis of the multicentre, double-blind, phase 3 randomised controlled trial *Lancet Oncology*

Cristofanilli.pdf

We appreciate the Panel's thorough consideration of Pfizer's recommendation that the indication for IBRANCE (palbociclib) in combination with fulvestrant be updated to state:

  - for postmenopausal women or pre menospausal women receiving ovarian suppression with an LHRH agonist with hormone receptor positive and HER2 negative metastatic breast cancer that has progressed *on or after prior adjuvant or metastatic endocrine therapy*

Kind regards,

Lynn L. McRoy, MD FACS
Senior Medical Director, US Medical Affairs Breast Cancer Team