

March 13, 2017

Submission Request
National Comprehensive Cancer Network[®] (NCCN[®])

RE: Clinical Evidence in Support of KISQALI[®] (ribociclib) in HR+/HER2- Breast Cancer

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NCCN Guidelines Panel: Breast Cancer

To Whom It May Concern:

As the NCCN Breast Cancer Panel reviews the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology[®] (NCCN Guidelines[®]) for Breast Cancer v.1.2017 and the associated Drugs and Biologics Compendium[™], we have enclosed data relating to treatment with KISQALI[®] (ribociclib) for your consideration:

- Data to support the use of ribociclib in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor positive, human epidermal growth factor receptor-2 negative (HR+/HER2-) advanced or metastatic breast cancer.

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Ribociclib plus an aromatase inhibitor for first-line treatment of HR+/HER2- advanced breast cancer

This request is for the Panel to consider the inclusion of ribociclib in combination with an aromatase inhibitor as a treatment option in section BINV-N of the Breast Cancer Guidelines and the associated NCCN Drugs and Biologics Compendium[™].

Data from the preplanned interim analysis of the Phase III study, Mammary ONcology Assessment of LEE011's (ribociclib) Efficacy and Safety-2 (MONALEESA-2), demonstrated that the combination of ribociclib plus letrozole was superior to treatment with letrozole alone in prolonging progression-free survival (PFS) (hazard ratio = 0.56, 95% CI: 0.43-0.72, $P = 3.29 \times 10^{-6}$). This benefit of improvement in PFS was also seen across all prespecified subgroup analyses. At the time of the data cutoff, the median duration of PFS was not yet reached in the ribociclib arm since 58% of patients were still on treatment (95%CI: 19.3 – not yet reached) versus 14.7 months (95%CI: 13.0 - 16.5) in the placebo arm.¹

Adverse events of any grade ($\geq 35\%$ of the patients in either arm) were neutropenia (74.3% and 5.2%), nausea (51.5% and 28.5%), infections (50.3% and 42.4%), fatigue (36.5% and 30.0%), and diarrhea (35.0% and 22.1%) in the ribociclib and placebo arms, respectively. The most common Grade 3 or 4 adverse events that were reported in $> 10\%$ of the patients in either arm were neutropenia (59.3% and 0.9%) and leukopenia (21.0% and 0.6%) in the ribociclib and placebo arms, respectively. The rates of study discontinuation due to adverse events were 7.5% in the ribociclib arm and 2.1% in the placebo arm.¹

Specific changes recommended for the Guidelines & Compendium

- Please include ribociclib in combination with an aromatase inhibitor as an endocrine therapy option for the treatment of HR+/HER2- postmenopausal women with recurrent or stage IV breast cancer in section BINV-N and update relevant discussion sections.
- Please consider adding ribociclib in combination with an aromatase inhibitor to the treatment algorithm (BINV-20) for ER and/or PR positive / HER2-, no prior endocrine therapy within 1 year, postmenopausal women.

FDA status

Ribociclib is approved in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with HR+/HER2- advanced or metastatic breast cancer.

Rationale for recommended change

Based on the FDA-approved labeled indication and data from the MONALEESA-2 study, ribociclib plus letrozole has demonstrated significantly longer PFS compared to letrozole alone.

Literature support

¹ Hortobagyi GN, Stemmer SM, Burris HA, et al. Ribociclib as first-line therapy for HR-positive, advanced breast cancer. N Engl J Med. 2016;375(18):1738-1748.
doi: 10.1056/NEJMoa1609709.

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We appreciate the opportunity to provide this additional information for consideration by the NCCN Breast Cancer Panel. If you have any questions or require additional information, please do not hesitate to contact me at 1-862-778-5494 or via e-mail at Neilda.baron@novartis.com. Thank you for your time and consideration.

Sincerely,

Neilda Baron, MD
Executive Director, Medical Information Oncology
Novartis Pharmaceuticals Corporation

Enclosures: Copy of Prescribing Information and referenced primary literature; Author disclosures within included references