

June 15, 2018

Submission Request  
National Comprehensive Cancer Network® (NCCN®)

**RE: Clinical Evidence in Support of the Combination of Tafinlar® (dabrafenib) and Mekinist® (trametinib) in Previously Untreated *BRAF V600E* Metastatic Non-Small Cell Lung Cancer**

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Date of request: June 15, 2018  
NCCN Guidelines Panel: Non-small Cell Lung Cancer (NSCLC)

To Whom It May Concern:

As the NCCN NSCLC Panel reviews the Clinical Practice Guidelines in Oncology® (NCCN Guidelines®) for Non-small Cell Lung Cancer version 4.2018, we have enclosed data relating to treatment with the combination of Tafinlar® (dabrafenib) and Mekinist® (trametinib):

- Data supporting the combination of dabrafenib and trametinib for the treatment of previously untreated metastatic NSCLC with a *BRAF V600E* mutation

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**Dabrafenib and trametinib for *BRAF V600E* advanced or metastatic NSCLC**

In the previously untreated arm (Cohort C) of the Phase II, multicenter, non-randomized, open-label study (N=36), patients receiving the combination of dabrafenib and trametinib achieved a median investigator-assessed progression-free survival (PFS) of 10.9 months (95% CI: 7-16.6 months) and median independent review committee-assessed PFS of 14.6 months (95% CI: 7.0–22.1).<sup>1</sup>

All patients had at least one adverse event (AE) of any Grade, most commonly (>30% of patients) pyrexia, nausea, diarrhea, fatigue, peripheral edema, decreased appetite, dry skin, and vomiting. Most common Grade 3/4 AEs were pyrexia (11%), increased alanine aminotransferase (11%), hypertension (11%) and vomiting (8%).<sup>1</sup>

**Specific changes recommended for the Guidelines & Compendium**

Please consider modifying the *BRAF V600E* Mutation Positive section (NSCL-25) to remove the footnote which states: “At this point, there are no published data on the progression free survival (PFS) of patients treated in the first line setting”.

**FDA status**

Dabrafenib in combination with trametinib is indicated for the treatment of patients with metastatic non-small cell lung cancer with *BRAF V600E* mutation as detected by an FDA-approved test.

Dabrafenib in combination with trametinib is indicated for the treatment of patients with unresectable or metastatic melanoma with *BRAF V600E* or *V600K* mutations as detected by an FDA-approved test. Dabrafenib and trametinib are also approved as single agents for the treatment of unresectable or metastatic melanoma with *BRAF V600E* or *V600E/K* mutation, respectively.

Dabrafenib in combination with trametinib is indicated, for the adjuvant treatment of patients with melanoma with *BRAF V600E* or *V600K* mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection.

Dabrafenib in combination with trametinib is indicated for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer with *BRAF V600E* mutation and with no satisfactory locoregional treatment options.

**Rationale for recommended change**

The results of this study have demonstrated the safety and efficacy, including PFS, of the combination of dabrafenib and trametinib in patients with advanced or metastatic NSCLC with a *BRAF V600E* mutation.<sup>1</sup>

**Literature support**

1. Planchard D, Smit E, Groen H, et al. Dabrafenib plus trametinib in patients with previously untreated *BRAF V600E*-mutant non-small-cell lung cancer: an open-label, phase 2 trial. *Lancet Oncol.* 2017 Oct;18(10):1307-1316.

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We appreciate the opportunity to provide this additional information for consideration by the NCCN NSCLC Panel. If you have any questions or require additional information, please do not hesitate to contact me at 862-778-5494 or via e-mail at [neilda.baron@novartis.com](mailto:neilda.baron@novartis.com).

Thank you for your time and consideration.

Sincerely,

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

Enclosures: Copy of referenced publication and Tafinlar and Mekinist Prescribing Information