July 8, 2020

Submission Request
National Comprehensive Cancer Network® (NCCN®)

RE: Clinical Evidence in Support of Capmatinib in Patients with High-level *MET*-amplified Advanced Non-Small Cell Lung Cancer

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NCCN Guidelines Panel:	Non-Small Cell Lung Cancer

To Whom It May Concern:

As the Panel reviews the NCCN Clinical Practice Guidelines in Oncology® (NCCN Guidelines®) for Non-Small Cell Lung Cancer (NSCLC) v.6.2020 and the associated Drugs & Biologics Compendium™, we are enclosing recent data related to Tabrecta™ (capmatinib) use in patients with high-level *MET*-amplified advanced NSCLC for your consideration[1]:

- Data from GEOMETRY mono-1 to support the use of capmatinib in adult patients with high-level MET-amplified (gene copy number [GCN] ≥10) advanced NSCLC.

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Capmatinib for the treatment of high-level *MET*-amplified advanced NSCLC

GEOMETRY mono-1 (NCT02414139) is a Phase II multi-cohort study that evaluated capmatinib 400 mg twice daily in patients with *MET*-amplified and *MET*ex14-mutated advanced NSCLC (N = 334). Patient cohorts were based on *MET* dysregulation status and prior treatment. Two cohorts of patients with high-level ([GCN] ≥10) *MET*-amplified NSCLC were analyzed:

- Cohort 1a - pretreated with 1 or 2 prior systemic lines
- Cohort 5a - treatment-naive

The primary endpoint is overall response rate (ORR) per RECIST 1.1 by Blinded Independent Review Committee (BIRC) assessment. The key secondary endpoint is duration of response (DOR) as assessed by BIRC.[1]

The efficacy summarized for Cohorts 1a and 5a have a data cut-off date of January 6, 2020. There were 84 patients evaluable; Cohort 1a (n = 69, 2nd/3rd line capmatinib) and Cohort 5a (n = 15, 1st line capmatinib). The ORR as assessed by the BIRC was 29% (95% CI, 18.7 - 41.2) in Cohort 1a and 40% (95% CI, 16.3 - 67.7) in Cohort 5a. The median DOR as assessed by the BIRC was 8.31 months (95% CI, 4.17 – 15.44) in Cohort 1a and 7.54 months (95% CI, 2.56 – 14.26) in Cohort 5a. At the data cut-off, there were three patients ongoing in Cohort 1a and none in Cohort 5a.[1]

In the overall study population (N = 334), the most common adverse reactions (≥20%) reported with capmatinib are peripheral edema, nausea, fatigue, vomiting, dyspnea, and decreased appetite. Serious adverse reactions occurred in 51% of patients who received capmatinib. Serious adverse reactions in ≥2% of patients included dyspnea (7%), pneumonia (4.8%), pleural effusion (3.6%), general physical health deterioration (3%), vomiting (2.4%), and nausea (2.1%). A fatal adverse reaction occurred in one patient (0.3%) due to pneumonitis.[2]

Specific changes recommended for the Guidelines & Compendium
Please consider including capmatinib as a treatment option for patients with high-level *MET*-amplified advanced NSCLC on the NSCL-H page and associated Discussion section.

FDA status
Capmatinib is a kinase inhibitor indicated for the treatment of adult patients with metastatic non-small cell lung cancer whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping as detected by an FDA-approved test.[2]

Rationale for recommended changes
Based on data from Cohorts 1a and 5a of the GEOMETRY mono-1 study, capmatinib demonstrated clinical activity in patients with high-level *MET*-amplified advanced NSCLC.

Literature support

1. Wolf J, Overbeck T, Han JY, et al. Capmatinib in patients with high-level MET-amplified advanced non-small cell lung cancer (NSCLC): results from the phase 2 GEOMETRY mono-1 study. *J Clin Oncol.* 2020; 38; (suppl; abstr 9509) 10.1200/JCO.2020.38.15_suppl.9509.
2. Tabrecta [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2020.

We appreciate the opportunity to provide this information for consideration by the NCCN Non-Small Cell Lung 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 email at neilda.baron@novartis.com.

Thank you for your time and consideration.

Sincerely,

Neilda Baron, MD
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Novartis Pharmaceuticals Corporation

Enclosures: Prescribing Information and referenced primary literature; author disclosures included within references.