November 4, 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.8 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

This request is for the Panel to consider inclusion of capmatinib as a treatment option for high-level *MET*-amplified advanced NSCLC in the Non-Small Cell Lung Cancer Guidelines® and the associated Drugs & Biologics Compendium.®

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 = 364). Patient cohorts were based on *MET* dysregulation status and prior treatment. Patients with high-level ([GCN] ≥10) *MET*-amplified NSCLC were analyzed in the following cohorts:

- Cohort 1a – pretreated with 1 or 2 prior lines, n = 69
- Cohort 5a – treatment-naive, n = 15
- Cohort 6 – pretreated with 1 prior line, n = 3

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 below for Cohorts 1a, 5a and 6 (GCN≥10) has a data cut-off date of January 6, 2020. The ORR as assessed by the BIRC was 29% (95% CI, 19-41) in Cohort 1a, 40% (95% CI, 16-68) in Cohort 5a and 0 in Cohort 6. However, the results did not meet the prespecified threshold for significance. The three patients in Cohort 6 had stable disease. The median DOR as assessed by the BIRC was 8.3 months (95% CI, 4.2-15.4) in Cohort 1a and 7.5 months (95% CI, 2.6-14.3) in Cohort 5a.[1]

In the overall study population (N = 364), the most common adverse events (>20% across all cohorts) reported with capmatinib were peripheral edema (51%), nausea (45%), vomiting (28%), increased blood creatinine (24%), dyspnea (23%), fatigue (22%), and decreased appetite (21%). The adverse event profile in Cohort 1a, 5a, and 6 were consistent with the overall study population.[1]

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 within the associated Discussion section.

FDA status
Capmatinib is not FDA approved for use in high-level *MET*-amplified advanced NSCLC. [2]

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]

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). [2]

Rationale for recommended changes
Capmatinib demonstrated clinical activity in patients with high-level *MET*-amplified advanced NSCLC in GEOMETRY mono-1.

Literature support

1. Wolf J, Seto T, Han JY, et al. Capmatinib in MET Exon 14-Mutated or MET-Amplified Non-Small-Cell Lung Cancer. *N Engl J Med*. 2020 Sep 3;383(10):944-957. doi: 10.1056/NEJMoa2002787.
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.