Name: Kirk Taylor, MD
Company/Organization: EMD Serono, Inc.
Address: One Technology Place, Rockland, MA 02370
Phone: 781-490-0455
Email: kirk.taylor@emdserono.com
Date of request: February 4, 2021

Dear NCCN Guidelines Panel Members,

On behalf of EMD Serono, Inc., I respectfully request the NCCN Non-Small Cell Lung Cancer Panel (NSCLC) to consider the recent FDA approval[1] and the pivotal clinical trial data[2-5] supporting the use of Tepotinib for the treatment of advanced or metastatic NSCLC with *MET* exon 14 skipping mutation.

Suggested Changes: We request the panel consider the following:

- **NSCL-28 –** "*MET* exon 14 skipping mutation discovered prior to first-line systemic therapy"
  - **"First-line therapy": please add "Tepotinib" as preferred**
  - **"Subsequent therapy": please add "Tepotinib" as preferred**
- **NSCL-28 –** "*MET* exon 14 skipping mutation discovered during first-line systemic therapy"
  - **"First-line therapy": please add "Tepotinib" as preferred**
- **NSCL-I (1 of 2) –** "Targeted Therapy or Immunotherapy for Advanced or Metastatic Disease"
  - **"*MET* Exon 14 Skipping Mutation": please add "Tepotinib" as preferred**

FDA Clearance[1]: Tepotinib is a kinase inhibitor indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (*MET*) exon 14 skipping alterations. Tepotinib was previously granted orphan-drug designation by the FDA for the treatment of NSCLC with MET genomic aberrations.

Rationale Summary: Tepotinib is a once-daily, orally-dosed, MET kinase inhibitor approved by the FDA based on the VISION Phase 2 clinical trial in patients with advanced or metastatic NSCLC with a confirmed *MET* exon 14 skipping mutation. Tepotinib demonstrated efficacy in both treatment-naïve and previously treated patients, with or without brain metastases, as well as across histologic subtypes, including adenocarcinoma, squamous cell carcinoma, and sarcomatoid carcinoma. Overall response rate was 46% (55% for patients with brain metastases) with a median progression-free survival of 8.5 months and a clinically manageable safety profile.[2,3]

Supporting Literature:
The pivotal Phase 2 VISION clinical trial studied tepotinib in 152 adult patients with *MET* exon 14 skipping mutation determined by liquid biopsy and/or tissue biopsy who have advanced or metastatic NSCLC. All patients were negative for *EGFR* mutations and *ALK* rearrangement. Results have been published with at least 9 months of follow-up in the *New England Journal of Medicine*.[2] The overall objective response rate reported by the independent review committee (IRC) was 46% with no

EMD Serono, Inc
One Technology Place
Rockland, MA 02370
Tel. +1(800) 283 8088
emdserono.com

significant difference among patients based on prior number of therapy, including patients who had received immunotherapy. Stable disease was reported in 19.2% of patients for a disease control rate (DCR) of 65.7%. Median duration of response (DOR) was 11.1 months and median duration of progression-free survival (PFS) was 8.5 months. Tepotinib also showed significant efficacy in patients with brain metastases, with 55% ORR and 10.9 months median PFS.[2]
The above results were confirmed in the updated pre-planned analysis of 146 patients, with an ORR of 45.2% (57.1% for patients with brain metastases), median DOR of 11.1 months, and median PFS of 8.9 months as determined by the IRC.[3,4] In addition, patient-reported outcomes showed a meaningful improvement in symptoms of cough and stable dyspnea and chest pain during the 24-week treatment.[5]

Tepotinib was generally well-tolerated. In the published data set, grade 3 or higher treatment-emergent adverse events (TEAEs) occurred in 28% of patients, with peripheral edema being the most common (7%).[2] Treatment discontinuation rate due to adverse events was 11%. There were 21 patients who had adverse events leading to death while on treatment, with one treatment-related death by respiratory failure and dyspnea secondary to interstitial lung disease.[2]

Based on the FDA approval and study data, we request the NCCN Non-Small Cell Lung Cancer Panel to consider inclusion of tepotinib as a preferred option for the first-line and subsequent treatment of *MET* exon 14 skipping mutation NSCLC in patients with metastatic or advanced disease.

Respectfully submitted,

DocuSigned by:
Kirk Taylor
7A5185F85F374AB...

Kirk Taylor, M.D.
Sr. Vice President
North American Medical Affairs
EMD Serono, Inc.

References:

1. TEPMETKO® (tepotinib) prescribing information. EMD Serono, Inc.
2. Paik et al. Tepotinib in Non–Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations. *N Engl J Med.* 2020; 383:931-943
3. Mazieres et al. Tepotinib in patients with advanced NSCLC with MET exon 14 skipping: Overall efficacy results from VISION Cohort A. Presented at the European Society for Medical Oncology, Sep 19-21, 2020. Poster 1283P.
4. Viteri S, et al. Activity of tepotinib in brain metastases: Preclinical models and clinical data from patients with MET exon 14 skipping NSCLC. Presented at the European Society for Medical Oncology, Sep 19-21, 2020. Poster 1286P.
5. Garassino et al. Health-related quality of life in patients with NSCLC harboring MET exon 14 skipping treated with tepotinib. Presented at the European Society for Medical Oncology, Sep 19-21, 2020. Poster 1347P.