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Dear Joan McClure, MS

Senior Vice President,
Clinical Information & Publications

National Comprehensive Cancer Network (NCCN)

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Date: February 18, 2015

Dear Ms. McClure,

We are writing to petition NCCN to continue the revision of its Guidelines and Compendium with respect to the use of unproven biological agents in the treatment of non-small cell lung cancer (NSCLC). We are supportive of some of the clarifications introduced in chart NSCLC-H in the recent version 4.2015, and we are encouraged by the downgrade of trastuzumab and afatinib to category 2B in her-2-positive NSCLC, and for cabozantinib's reclassification to 2B for RET rearrangements. However, the continued 2A classification of vemurafenib and dabrafenib for BRAF V600E mutations, and crizotinib for MET amplifications and ROS1 rearrangements, remains highly questionable in view of the lack of the supportive level 1 scientific data.

Specific Changes:

1. Vemurafenib and dabrafenib should not be designated as category 2A agents for BRAF V600E mutations in NSCLC.
2. Crizotinib should not be designated as category 2A agents MET amplifications and ROS1 rearrangements in NSCLC.

FDA Clearance: Vemurafenib and dabrafenib are not FDA approved for BRAF V600E mutations in NSCLC. Crizotinib is not FDA approved for MET amplifications and ROS1 rearrangements in NSCLC.

Rationale for recommended change: Lack of level 1 peer-reviewed data or FDA approval.

References:

1. Gautschi O et al. A patient with BRAF V600E lung adenocarcinoma



- responding to vemurafenib. J Thorac Oncol. 2012;7:e23-24.
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 3. Ou SH et al. Activity of crizotinib (PF02341066), a dual mesenchymal-epithelial transition (MET) and anaplastic lymphoma kinase (ALK) inhibitor, in a non-small cell lung cancer patient with de novo MET amplification. J Thorac Oncol. 2011;6:942-946.
 4. Camidge DR et al. Efficacy and safety of crizotinib in patients with advanced c-MET-amplified non-small cell lung cancer (NSCLC). J Clin Oncol (Meeting Abstracts) 2014;32:15_suppl 8001.
 5. Bergethon K et al. ROS1 rearrangements define a unique molecular class of lung cancers. J Clin Oncol. 2012;30:863-870.
 6. Shaw AT et al. Crizotinib in ROS1-rearranged non-small-cell lung cancer. NEJM 2014;371;1963-1971.
 7. Johnson DH et al. Recent clinical advances in lung cancer management. J Clin Oncol. 2014 Apr 1;32(10):973-82.

Sincerely,

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