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Date of request: May 26, 2021
NCCN Guidelines Panel: Non-Small Cell Lung Cancer

On behalf of Illumina, I respectfully request the NCCN Guideline Panel for Non-Small Cell Lung Cancer to consider the requested updates pertaining to the evaluation of patients with non-small cell lung cancer.

Specific Changes (in red text)**:**

1. (NSCL-18) Amend the second sub-bullet point under Biomarker Testing, Molecular testing, to Testing should be conducted as part of broad molecular profiling to include comprehensive genomic profiling by a validated and/or FDA-approved test[mm] (Note there are 2 places on NSCL-18)

2. (NSLC-18) Amend footnote mm to The NCCN NSCLC Guidelines Panel strongly advises broader molecular profiling including comprehensive genomic profiling by a validated and/or FDA approved test with the goal of identifying rare driver mutations for which effective drugs may already be available, or to appropriately counsel patients regarding the availability of clinical trials. ~~Broad molecular profiling~~ Comprehensive genomic profiling is a key component of the improvement of care of patients with NSCLC. See Emerging Biomarkers to Identify Patients for Therapies (NSCL-I).

Rationale:

Currently the guideline refers to the molecular testing of multiple gene mutations at once as 'broad molecular profiling'. Broad molecular profiling can vary widely. Comprehensive genomic profiling (CGP) is a modality for performing broad molecular profiling.

The most commonly used definition of CGP can be found on the CMS website.[1] It defined CGP as providing additional insight beyond individual gene hotspots provided by NGS-based Targeted Tumor Panels that identify somatic alterations known to occur in certain regions (i.e., "hotspot") within specific genes of interest. "[CGP] typically involves sequencing of entire exonic regions of genes of interest […], and may also include selected intronic regions".

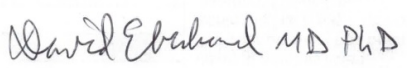
The distinction made between different types of NGS assays, and the types of biomarkers that they are suited to assess, is based on scientific evidence.[2-3] However, many oncologists in practice may not be familiar with the technical details of complex NGS assays and the differences between them. Consistent language describing NGS assays and broad molecular profiling may increase physician awareness of the differences between complex tests and improve access to appropriate testing and subsequent treatment.[4] Therefore, we ask that NCCN incorporate terminology that aligns more closely with the one presented by CMS and the testing manufacturers.

The following articles are submitted in support of this proposed change.

1. Medicare Coverage Database: Local Coverage Article, Billing and Coding: MolDX Targeted and Comprehensive Genomic Profile Next Generation Sequencing Testing in Cancer (A54901)https://www.cms.gov/medicare-coverage-database/details/article-details.aspx?articleId=54901&ver=9&LCDId=36021&Date=&DocID=A56973&bc=gQAAAAIAIAAA&

2. Merino DM, McShane LM, Fabrizio D, et al. Establishing guidelines to harmonize tumor mutational burden (TMB): in silico assessment of variation in TMB quantification across diagnostic platforms: phase I of the Friends of Cancer Research TMB Harmonization Project. *J Immunother Cancer* 2020;8:e000147.
3. Buchhalter, I. Size matters: Dissecting key parameters for panel-based tumor mutational burden analysis. *Int J Cancer*, 2019 Feb 15;144(4):848-858.
4. Emerging Biomarkers to Identify Novel Therapies for Patients with Metastatic NSCLC, NSCL-I, https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1450

Thank you for your consideration,



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