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NCCN Guidelines Panel: NSCLC

Dear Panel Members,

On behalf of Foundation Medicine, I respectfully request the NCCN® Non-Small Cell Lung Cancer (NSCLC) Guidelines Panel consider the requested updates pertaining to the evaluation and management of patients with NSCLC.

Requested Update and Rationale:

Define "broad molecular profiling" as inclusive of large validated NGS panels (>50 genes and comprehensive genomic profiling (CGP)) in footnote (kk) on page NSCL-18A.

CGP can efficiently detect individual gene (eg. *EGFR*, *ALK*, *ROS1*, *BRAF*, *KRAS*, *NTRK*, *MET*, *RET*, *ERBB2*) alterations, tumor mutational burden (TMB), and MSI status using a single sample[1]. This allows conservation of tissue while obtaining as much information as possible to inform the use of currently available biomarker driven therapies and immunotherapies and define/refine clinical trial options. Accurate measurement of TMB is achieved through whole exome sequencing (WES) or targeted NGS assays which analyze greater than 1 megabase of DNA, at least several hundred genes, and have been validated against WES or a targeted NGS assay that has been FDA-approved specifically for TMB measurement and reporting per the recommendations published by the Friends of Cancer Research TMB Harmonization Project[2-5]. **Clarifying the definition of "broad molecular profiling" as inclusive of larger validated NGS based panels (>50 genes) and CGP will increase access to these testing methodologies for patients diagnosed with advanced NSCLC.**

Thank you for your review of this submission.

Sincerely,

Brian Alexander, M.D.
Chief Medical Officer
Foundation Medicine

References

1. FoundationOne CDx Technical Information. attached
2. Chalmers ZR, Connelly CF, Fabrizio D, et al. Analysis of 100,000 human cancer genomes reveals the landscape of tumor mutational burden. Genome Med 2017;9:1–14.
3. US FDA SSED FoundationOne CDx https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P170019S016
4. Zehir A, Benayed R, Shah RH, et al. Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients. Nat Med 2017;23:703–13.
5. 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.