November 13, 2021

National Government Services (NGS)
Medical Policy Unit
P.O. Box 7108
Indianapolis, IN 46207-7108
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Re: Public Comments for Proposed Local Coverage Determination, "Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms (DL37810)"

Submitted electronically

Dear National Government Services:

On behalf of LUNGevity Foundation, the nation's preeminent lung cancer nonprofit that funds research, provides education and support, and builds communities for the approximately 236,000 Americans diagnosed with lung cancer each year[1] and the 541,000 Americans living with the disease,[2] we appreciate the opportunity to submit our comments in response to the Proposed Local Coverage Determination on Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms (DL37810).

LUNGevity is a leading patient advocacy group that represents the voice and interests of the national lung cancer survivor community by accelerating patient-centered, empowering patients to be active participants in their treatment and care decisions and identifying and helping remove access barriers to high quality care. As such, LUNGevity applauds National Government Services (NatGov) for proposing to cover Next Generation Sequencing Comprehensive Genomic Profiling (NGS CGP) for patients with advanced cancer as this is standard of care for many patients with lung cancer.

Biomarker testing, typically through comprehensive genomic profiling (such as NGS) and testing for protein markers (such as PD-L1 for immunotherapy), is the first step to accessing personalized medicine. Timely access to diagnostics that inform treatment decisions is critical for all patients, especially those with cancer. In this era of unprecedented scientific advancements for the treatment of lung cancer, patients diagnosed today have the advantage, opportunity, and right to know their tumor's unique biomarker profile to help them and their care team identify the most appropriate treatment option(s). Our comments provided below reiterate LUNGevity's stand on the importance of access to timely biomarker testing, ideally through comprehensive tests such as NGS.

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, making up 85% of lung cancer cases.[3,4] The complex nature of this disease requires personalized management plans for patients.[4] Since the discovery of the first epidermal growth factor receptor (EGFR) mutation in lung cancer in 2004, targeted therapies have become a major component of the treatment arsenal for NSCLC patients.[5-9] At least 10 driver mutations in lung adenocarcinoma have been identified (EGFR, ALK, ROS, RET, ERB2/HER2 mutations, ERB2/HER2 amplifications, MET amplifications, MET mutations, TRK, BRAF, KRAS).[8-11] In concert with the identification of an increasing number of targetable mutations is the development of novel, potent, and specifically targeted therapies. For example, at present, third generation EGFR[12] tyrosine kinase inhibitors (TKIs) and anaplastic lymphoma kinase (ALK) TKIs[13] are used in clinical practice. With the increased use of targeted agents has come the problem of acquired resistance, where cancer cells inevitably develop resistance to the targeted agent. Indeed, lung cancer is now leading the field of precision medicine where research is rapidly progressing to develop better targeted therapies and combat mechanisms of resistance.

Recommended changes to the proposed LCD:

LUNGevity agrees with the evidence that was outlined in the proposed LCD to support the use of NGS in NSCLC patients as it provides the best opportunity for optimal clinical outcomes. However, we propose some changes to the current LCD language to improve access to NGS for advanced stage cancer patients:

Expanding the one test per primary cancer limit for NGS:

Access to high-quality, timely NGS testing (at diagnosis and at recurrence or progression) is instrumental for matching patients to the appropriate targeted therapy and advancing precision medicine.

New evidence clearly establishes the value of multiple NGS tests throughout the duration of a patient's treatment journey. An NGS panel at the **time of diagnosis** (**primary cancer before first-line treatment is initiated**) and subsequent NGS panels at **recurrence/progression** on first and subsequent lines of therapy fulfill similar and unique purposes.

NGS at diagnosis: An NGS panel at the time of diagnosis simultaneously checks for multiple clinically actionable mutations that help guide physicians to targeted therapies to treat NSCLC.[14] This, in turn, enables timely matching of the patient to the right targeted therapy should a targetable mutation be present. The National Comprehensive Cancer Network (NCCN) guidelines recommend multiplex testing such as NGS platforms for making treatment decisions.[15]

NGS at progression or recurrence: It is now well established that tumors evolve with time in response to targeted therapies.[16] These new molecular alterations confer acquired resistance to targeted therapies and are responsible for progression or recurrence after a patient has

received first-line targeted treatments. An NGS panel at the time of progression or recurrence helps identify these new mechanisms of resistance or tumor heterogeneity after treatment with a targeted agent, **often independent of the original driver mutation detected at the time of diagnosis**. In the recent FLAURA trial of first-line osimertinib in EGFR-positive NSCLC, NGS assays at the time of progression helped identify additional mechanisms of resistance such as a C797S mutation in the EGFR gene and mutations in the PIK3CA and the MET genes.[17,18] Currently, drugs targeting MET amplification or PIK3CA are in clinical development and there is evidence suggesting that EGFR C797S is sensitive to first-generation EGFR inhibitors such as erlotinib. [17,19,20] This suggests that an NGS panel is ideal for determining the next line of treatment for an NSCLC patient who has progressed on a targeted agent and reiterates the importance of multiple NGS panels in a patient's lifetime.

As stated above, new mutations in NSCLC are being discovered very quickly and limiting access to one test per a patient's lifetime for a single primary cancer may be detrimental to their treatment and could both prevent their physicians from identifying the accurate first-line targeted therapy that may save their life and impede access to subsequent lines of therapy.

One of the crucial benefits of NGS testing is allowing a complete molecular profile of the patient's tumor before first-line treatment initiation and after treatment(s) and allowing novel classes of drugs to be offered to the patient as their tumor evolves. Offering an NGS panel at the time of diagnosis and at recurrence or progression also allows for identifying driver mutations that have drugs in clinical development both as first-line treatment options and at progression or recurrence, thereby allowing patients to be enrolled rapidly in clinical trials. This is especially crucial since NCCN guidelines suggest that clinical trials may often offer the best treatment option in first- and subsequent-line settings.[15]

Please remove: "CGP for NGS patient with advanced cancer is reasonable and necessary only when more limited (e.g. individual analyte or targeted panel (5-50 genes)) testing is insufficient.

As noted above, comprehensive biomarker testing/ genomic profiling is standard of care, and lifesaving, for many patients with lung cancer across the continuum of care. Single analyte testing can cause delays in diagnosis and care and can also waste a patient's tumor tissue, a very valuable resource.

LUNGevity is grateful for the opportunity to comment on the above-captioned LCD and is eager to work with National Government Services to continue to ensure that patients have timely access to high-quality biomarker testing.

The recommendations outlined above can be discussed with me, my staff, and LUNGevity's Scientific Advisory Board, which is made up of some of the world's leading experts in lung cancer biology, practice management, access to innovative medicines, and overall patient care.

I can be reached at 240-454-3100 or aeferris@lungevity.org if you have any questions or would like to engage in further dialogue.

Thank you for your attention to this very important matter.

Sincerely,

Andrea Stern Ferris
President and Chief Executive Officer
LUNGevity Foundation

ABOUT LUNGEVITY:

LUNGevity's mission is to improve outcomes for people diagnosed with lung cancer. Our goals are three-fold: (1) to accelerate research to patients that is meaningful to them; (2) to empower patients to be active participants in their care and care decisions; and (3) to help remove barriers to access to high quality care. We have the largest lung cancer survivor network in the country and actively engage with them to identify, understand, and address unmet patient needs. We also have a world class Scientific Advisory Board that guides the programs and initiatives of the organization. Additionally, we collaborate with other lung cancer patient advocacy groups and organizations, such as the American Lung Association and CHEST, who serve the lung cancer community.

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