LUNGEVITY
Find it. Treat it. Live.

May 9, 2018

Dr. James Almas
Medical Director
MolDX
17 Technology Circle
AG-315
Columbia, SC 29202

Dear Dr. Almas:

On behalf of LUNGevity Foundation, the nation's preeminent lung cancer nonprofit that funds research, provides education and support, and builds communities for the 222,500 Americans diagnosed with lung cancer each year and the 527,228 Americans living with the disease, we appreciate the opportunity to submit our comments in response to the proposed/draft Local Coverage Determination (LCD) for Guardant360 Plasma-Based Comprehensive Genomic Profiling in Non-Small Cell Lung Cancer (NSCLC) (DL37699).

As a leading patient advocacy group that represents the voice and interest of the national lung cancer survivor community by accelerating research to patients that is meaningful to them, empowering patients to be active participants in their care and care decisions, and helping remove barriers to access to high quality care, LUNGevity applauds MolDX for providing a coverage determination for the Guardant360 test and ensuring new testing options are available for lung cancer patients. In this era of unprecedented scientific advancements for the treatment of lung cancer, particularly in the field of biomarker testing, liquid biopsy tests, like Guardant360's, are a promising new development that identify markers predictive of response to particular treatments for patients in a convenient, low cost, and quickly-responsive manner.

Non-small cell lung cancer (NSCLC) is the more common type of lung cancer, diagnosed in about 85% of people with lung cancer.[1,2] The complex nature of this disease requires personalized management plans for patients.[2] 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 of NSCLC patient.[3-5] Now at least 10 driver mutations in adenocarcinoma have been identified (EGFR, ALK, ROS, RET, ERB2/HER2 mutations, ERB2/HER2 amplifications, MET amplifications, MET mutations, TRK, BRAF, KRAS).[6,7] In concert with the identification of an increasing number of targetable mutations is the development of novel, potent, and more specific targeted therapies. For example, at present, third generation EGFR[8] tyrosine kinase inhibitors (TKIs) and second generation anaplastic lymphoma kinase (ALK) TKIs[9] 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. The EGFR T790M is an excellent example of a resistance mutation that develops in patients treated with first- and

second-generation EGFR TKIs. This mutation can be rapidly detected using a liquid biopsy test such as the cobas EGFR Mutation Test v2.[10] Lung cancer is now leading the field of precision medicine where research is rapidly progressing to (1) develop better targeted therapies that combat mechanisms of resistance, and (2) noninvasive assays – such as liquid biopsies – that can monitor status of the resistance mutations (e.g., cobas EGFR Mutation Test v2), sequentially and in real time.[11]

The utility of liquid biopsies in the clinical management of lung cancer is unquestionable, because 1 out of 4 NCSLC patients may be ineligible for a solid tissue biopsy.[12] In her ASCO 2017 presentation on biomarker testing for lung cancer, LUNGevity Scientific Advisory Board (SAB) member, Dr. Alice Shaw from Massachusetts General Hospital, pointed out that liquid biopsies may help in (1) initial detection of targetable mutations in advanced-stage NSCLC at the time of diagnosis, (2) identification of acquired resistance mutations in patients who have relapsed on targeted therapies, and (3) monitoring response to targeted therapies and predicting outcome in advanced-stage NSCLC patient.[13]

Given the utility of liquid biopsy and monitoring importance, we request that you reconsider the "at progression section" of the coverage guidance to include access for ***all eligible advanced-stage*** NSCLC patient at progression rather than limiting it to select mutations. Treatment approaches of lung cancer is rapidly evolving, with third-generation tyrosine kinase inhibitors such as osimertinib, first approved in the post-progression setting, moving to the first-line setting for the treatment of EGFR-positive adenocarcinoma.[14, 15] The use of osimertinib in the first-line setting (FLAURA trial) offers a far superior median progression-free survival of 18.9 months versus 10.2 months median PFS offered by first- and second-generation EGFR TKIs.[14] With this progress has come the need to understand mechanisms of resistance to osimertinib in the first-line setting. In the FLAURA trial, mechanisms of resistance observed in nine patients studied includes a variety of genomic alterations (such as MET amplifications, PIK3CA mutations, or C797S mutations, for example) in the absence of an acquired T790M mutation. Despite the small sample size, this provocative data suggests that detection of resistance mutations such as PIK3CA or EGFR C797S in patients who have progressed on first-line osimertinib, using non-invasive approaches, may help determine second-line treatment options. 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.[15, 16, 17] Using a non-invasive test at the time of progression would not only be beneficial to the patient but also expedite the selection of second-line treatment options.

Last but not least, we request that you review the CPT/HCPC S Codes section of the proposed LCD and consider inclusion of the new ICD 10 code C34.90 (malignant neoplasm of unspecified part of unspecified bronchus or lung) that was created in 2017 in place of the ICD-9-CM 162.9 code. The ability to use this code will be extremely important for patient access, as often times the specific location of the originating tumor is unknown at time of biopsy.

As a leading patient advocacy group that represents the voice and interest of the national lung cancer survivor community, we are excited about the role of liquid biopsies in clinical management of NSCLC.

The discussion outlined above can be discussed with my staff, myself, and LUNGevity's SAB, 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 dialog.

LUNGevity is grateful for the opportunity to comment on this determination. 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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