



September 13, 2019

Seema Verma, Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Attention: CMS-1717-P
Mail Stop C4-26-05
7500 Security Boulevard
Baltimore, MD 21244-1850

Dear Administrator Verma,

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 230,000 Americans diagnosed with lung cancer each year and the 538,243 Americans living with the disease,¹ we appreciate the opportunity to submit our comments in response to the "Laboratory Date of Service Policy"(DOS) in the Centers for Medicare & Medicaid Services (CMS) Hospital Outpatient Prospective Payment System (HOPPS) Proposed Rule for Calendar Year 2020 issued on July 29, 2019.

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 was pleased to see the changes to the Date of Service Rule in the CY 2018 Hospital Outpatient Prospective Payment System Final Rule and is very thankful that CMS had taken into account concerns raised by stakeholders such as LUNGevity about the impact of the 14-Day rule on timely patient access to critical diagnostic testing. In contrast, LUNGevity is quite alarmed to see that CMS is now considering effectively rolling back the changes made in 2018 as outlined in the CY 2020 HOPPS Proposed Rule and our comments below are intended to outline why if implemented, such revisions would reinstitute access barriers to timely testing for lung cancer patients that the 2018 rule corrected, likely leading to suboptimal care. **Specifically, LUNGevity respectfully requests that CMS not finalize the "Changing the Test Results Requirement at 42 CFR 414.510(b)(5)(iv)" or "Limiting the Laboratory DOS Exception at 42 CFR 414.510(b)(5) to ADLTs" changes discussed in the DOS portion of the above referenced proposed rule due to the harmful impact on patient access to testing and resulting appropriate care.**

Delays in comprehensive biomarker testing are harmful to lung cancer patients

As drafted, the proposed rule would create unnecessary and harmful delays in biomarker testing, the first step to accessing personalized therapies. LUNGevity is specifically concerned



with potential impacts of the proposed physician certification component and the proposed limitation of the Laboratory DOS Exception to ADLTs. Requiring physicians to certify whether or not the results of a test would be used to guide hospital treatment at a subsequent encounter would not only create additional administrative burdens for providers and hospital systems, thereby creating or contributing to delays in testing, but it also is unclear to us exactly how a physician would be able to make such determination with any degree of certainty. Given that very few tests have been granted ADLT status, we are concerned with the proposal to limit the Laboratory DOS Exception to ADLTs as this would not capture many of the tests used in lung cancer, meaning that there would once again be delays in testing for lung cancer which would create undue harm.

Non-small cell lung cancer (NSCLC) is the more common type of lung cancer, diagnosed in about 85 percent of people with lung cancer.^{2,3} The complex molecular nature of this disease requires personalized management plans for patients.³ 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 patients.⁴⁻⁸ At present time, at least 10 driver mutations in adenocarcinoma have been identified (EGFR, ALK, ROS, RET, ERB2/HER2 mutations, ERB2/HER2 amplifications, MET amplifications, MET mutations, NTRK, BRAF, KRAS)⁷⁻¹⁰, five of which have FDA-approved targeted therapies.

Many lung cancer patients are able to benefit from targeted therapies to treat their cancer; however, in order to identify the appropriate therapy, it is essential that every individual diagnosed with lung cancer receive timely comprehensive biomarker testing to identify the most appropriate treatment plan for each unique individual. There is unequivocal evidence that targeted therapies, matched to a specific biomarker, are superior to chemotherapy, in improving survival of advanced-stage lung cancer patients. However, the complexities within the proposed DOS rule would likely lead to delayed biomarker testing as was the case previous to the CY 2018 rule change, once again limiting patient access to the test results required for physicians to identify and prescribe appropriately targeted life-saving and life-prolonging therapies, and ultimately creating longer than a 14-day delay for most lung cancer patients (due to the additional time required for a test to be run and results to be returned to the treating physician).

A report on biomarker testing practices in community cancer centers cites the former DOS rule in particular as a serious hurdle for appropriate genomic evaluation of non-small cell lung cancer (NSCLC), and these hurdles have consequences: "These challenges can lead to under genotyping, with a recent series reporting as much as 40% and 60% of patients without guideline recommended EGFR and ALK testing, respectively, and 19% receiving cytotoxic chemotherapy before test result review. These factors also lead to under referral to clinical trials of molecularly targeted agents."¹¹ A second study showed that even when appropriate tests are ordered, delays such as those that may arise due to the current DOS rule can affect treatment decisions. The researchers found that of the patients who received appropriate biomarker



testing prior to starting treatment, 79% of EGFR-positive patients and 94% of ALK-positive patients received the appropriate targeted therapy. In contrast, of the patients who did not receive their EGFR or ALK positive diagnoses until four or more weeks had elapsed [due to delays from holding a test for 14 days combined with the ~14 additional days needed by labs to run the test], only 41% of EGFR-positive patients and 65% of ALK-positive patients received an appropriate targeted therapy during their first line treatment.¹² In addition, delays in biomarker testing may not only impact the right treatment selection, but in fact, may lead to a patient getting matched to the **wrong** treatment. It is now well-documented that NSCLC patients with a driver mutation who receive an immune checkpoint inhibitor (ICI) **before they received a targeted therapy** show a much higher incidence of severe immune-related adverse events. This has been reported in patients with EGFR mutations receiving osimertinib after an ICI¹³; and in patients with oncogenic alterations in ALK, ROS1, or MET receiving crizotinib after an ICI¹⁴.

These data highlight the importance of receiving information from a comprehensive biomarker panel before the initiation of treatment for advanced-stage NSCLC patients.

The impact of changing the CY 2018 Date of Service Exemption on lives of patients cannot be underestimated

In addition, prior to the CY 2018 Date of Service Exemption, many lung cancer patients who were already facing a short life span and terminal diagnosis had to manage additional stress and unnecessary burden as a result of delays in testing and treatment due to the 14-day rule. In a recently published study on the increase in time to initiating cancer therapy and association with worsened survival, it was reported that “[t]ime to treatment initiation (TTI) has lengthened significantly over recent years, associated with multiple factors. Increase in TTI is associated with substantial increase in mortality ranging from 1.2–3.2% per week per week of delay in curative settings such as early-stage breast, lung and pancreas cancers.” Simplifying access to biomarker testing to shorten TTI, even in early-stage lung cancer patients, could have a significant impact on those mortality rates by increasing access to adjuvant treatments or adjuvant clinical trials with targeted therapies.¹⁵ Walking back the changes made in the CY2018 Final Rule would put more patients at risk of suffering unnecessary additional stress and burdens due to delays in testing.

As we did in 2017, we encourage CMS to continue to evaluate this policy at least annually to ensure that access barriers do not continue to exist and that patients are able to access the test of their and their physician’s choosing to ensure timely and accurate results. LUNGevity recommends that CMS take the necessary time to acquire meaningful data on the patient impact of the 2018 revisions to the DOS rule – which have been in place for less than 2 years – prior to implementing any additional changes to thoroughly understand the impact of these systematic changes.



In closing, LUNGeivity asks CMS to **not limit beneficiary access to timely and appropriate molecular pathology testing by not finalizing the above-referenced proposed changes to the DOS policy.**

LUNGeivity as well as other patient advocates and stakeholders were very thankful that CMS listened to stakeholder concerns in 2017 and were very pleased to see that the CY 2018 final rule protected patients from unnecessary delays in testing. LUNGeivity is thankful for the opportunity to comment on the changes to the Laboratory Date of Service Policy in the proposed rule and we truly hope that CMS once again will listen to the concerns of the broad stakeholder community, and especially to the patient advocacy community as it did in 2017. Once again, we encourage CMS **not to finalize** the above-referenced proposed changes as they will be harmful to patient access and will bring patients back to the pre-2018 world where access to timely and appropriate testing was limited and restricted by the 14-Day rule.

As always, the recommendations outlined above can be discussed with me, my staff, and LUNGeivity'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,

A handwritten signature in black ink, appearing to read "Andrea Stern Ferris".

Andrea Stern Ferris
President and Chief Executive Officer
LUNGeivity Foundation

ABOUT LUNGEVITY:

LUNGeivity'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.

REFERENCES:

1. SEER. Cancer Stat Facts: Lung and Bronchus Cancer. Available at <https://seer.cancer.gov/statfacts/html/lungb.html>. Accessed July 29 2019.
2. Thomas A, Liu SV, Subramaniam DS, et al. Refining the treatment of NSCLC according to histological and molecular subtypes. *Nat Rev Clin Oncol* 2015;12:511-526.
3. Johnson DH, Schiller JH, Bunn PA, Jr. Recent clinical advances in lung cancer management. *J Clin Oncol* 2014;32:973-982.
4. Lynch TJ, Bell DW, Sordella R, et al. Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib. *N Engl J Med* 2004;350:2129-2139.
5. Paez JG, Janne PA, Lee JC, et al. EGFR mutations in lung cancer: correlation with clinical response to gefitinib therapy. *Science* 2004;304:1497-1500.
6. Pao W, Miller V, Zakowski M, et al. EGF receptor gene mutations are common in lung cancers from "never smokers" and are associated with sensitivity of tumors to gefitinib and erlotinib. *Proc Natl Acad Sci U S A* 2004;101:13306-13311.
7. Doroshow DB, Herbst RS. Treatment of Advanced Non-Small Cell Lung Cancer in 2018. *JAMA oncology* 2018;4:569-570.
8. Herbst RS, Morgensztern D, Boshoff C. The biology and management of non-small cell lung cancer. *Nature* 2018;553:446-454.
9. Hirsch FR, Suda K, Wiens J, et al. New and emerging targeted treatments in advanced non-small-cell lung cancer. *Lancet* 2016;388:1012-1024.
10. Soo RA, Stone EC, Cummings KM, et al. Scientific Advances in Thoracic Oncology 2016. *Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer* 2017.
11. Gutierrez ME, Choi K, Lanman RB, et al. Genomic Profiling of Advanced Non-Small Cell Lung Cancer in Community Settings: Gaps and Opportunities. *Clin Lung Cancer* 2017.
12. Ruggiero JE, Rughani J, Neiman J, et al. Real-world concordance of clinical practice with ASCO and NCCN guidelines for EGFR/ALK testing in aNSCLC. Available at <http://meetinglibrary.asco.org/record/141019/abstract>. Accessed August 20 2017.
13. Schoenfeld AJ, Arbour KC, Rizvi H, et al. Severe immune-related adverse events are common with sequential PD-(L)1 blockade and osimertinib. *Annals of oncology : official journal of the European Society for Medical Oncology* 2019;30:839-844.
14. Lin JJ, Chin E, Yeap BY, et al. Increased Hepatotoxicity Associated with Sequential Immune Checkpoint Inhibitor and Crizotinib Therapy in Patients with Non-Small Cell Lung Cancer. *Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer* 2019;14:135-140.
15. Khorana AA, Tullio K, Elson P, et al. Time to initial cancer treatment in the United States and association with survival over time: An observational study. *PloS one* 2019;14:e0213209.