LUNGEVITY
Find it. Treat it. Live.

June 10, 2019

Steven, D. Pearson, MD MSc, FRCP
President, Institute for Clinical and Economic Review
Boston, MA 02109

Dear Dr. Pearson,

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 request for comments on ICER's 2020 Value Assessment Framework. We applaud ICER for providing stakeholders this opportunity to submit feedback prior to the release of the draft Value Assessment Framework and we encourage ICER to review all comments and reach out to stakeholders for more in-depth discussions of the comments prior to drafting the draft Value Assessment Framework.

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 are 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 and contributes to public comment letters such as this one.

In this era of unprecedented scientific advancements for the treatment of lung cancer, particularly personalized medicine and immunotherapy, we recognize the importance of balancing innovation with higher costs of medicines while ensuring that patients have access to life-saving therapies. We appreciate the work and the desire to create tools to facilitate the conversation between healthcare providers and patients around treatment options. We also recognize the incredible responsibility of ensuring that ALL stakeholders – ***especially patients*** – are fully represented in developing these tools and the utmost importance of including robust data that represents how the therapies are used in practice.

In summary, we recommend the following to make the ICER model more rigorous and patient-centric:

1. Incorporation of methodological and end-user transparency
2. Inclusion of patient experience and clinical practice perspective
3. Use of patient experience metrics that are not aggregate and capture the true meaningful benefit of a treatment approach, across the disease continuum of care
4. Integration of real-world evidence and real-world data into the ICER value assessment framework

These are discussed in greater detail below.

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1. **Incorporating both methodological and end-user transparency into the ICER model will make it more acceptable and robust.**

   Methodological transparency: We understand and appreciate the effort ICER has put in toward building a robust cost-effectiveness model and respect the proprietary nature of the effort; however, the lack of transparency calls into question its validity. Oncology value frameworks such as the ASCO Value Framework [2] and Memorial Sloan Kettering Drug Abacus [3] have made their methodology transparent, and we would encourage ICER to do the same.

   Given the rapid evolution of lung cancer therapies (there were seven new FDA approvals for lung cancer in 2015[4]), we encourage ICER to be fully transparent about the selection process of the drugs being evaluated (why are drugs that have not even been approved yet being included in the model?), the expert clinicians who are advising on the real-world use of the therapies, the model inputs and how the model will be used. At a minimum, we encourage that the models be peer reviewed by disease state experts.

   End-user transparency: ICER has maintained that the models developed are end-user-neutral and will not be used to make reimbursement or payment decisions. However, according to the Federal Register / Vol. 81, No. 48 / Friday, March 11, 2016 /Proposed Rules, Medicare payment model under section 1115A of the Social Security Act (the Act), CMS states, "We propose to use indications-based pricing where appropriately supported by published studies and reviews or evidenced-based clinical practice guidelines, such as the ICER reports, to more closely align drug payment with outcomes for a particular clinical indication." While this proposed model did not move forward, CMS' interest in using ICER reports causes much concern.

   We recommend that ICER recognize the impact of their models and ensure that they are created in a robust, evidence-based and patient-centric manner and recognize how their model may be used in clinical practice as well as to make reimbursement decisions.

2. **Including the patient experience will be invaluable in determining the true value of a treatment approach.**

   With progress in lung cancer treatment, survivors are living longer. It is imperative to incorporate the survivor perspective rather than make generalized statements about all people with lung cancer as the patient/survivor populations can be very different. Contrary to popular belief, lung cancer is becoming a disease of the young and the non-smoker. [5] A young, 30-year-old, stage IV survivor may value benefits from a treatment regimen very differently than a 70-year-old survivor. These nuances would be captured through **patient preference** studies and quality of life metrics which are often not included in existing clinical trial data.

   LUNGevity Foundation has spearheaded the first lung cancer advocacy-driven patient preference initiative. The initiative, *Project Transform*, is a multi-year, multi-stakeholder collaborative endeavor between LUNGevity and Ohio State University. It encompasses core principles of patient-centered outcomes research (PCOR), in line with LUNGevity's mission of providing a voice to the lung cancer

patient. The goal of *Project Transform* is to change the paradigm in lung cancer from assumptions being made about patients' wishes to evidence-based conclusions about patients' need and desires. Currently in its third year of a nationwide patient preferences survey, the project built its quantitative phase through a rigorous patient engagement model in which lung cancer patients provided direct feedback and input on the project implementation.[6,7] An important finding from the quantitative component showed that patients who had received 2 or more lines of therapies had different preferences than those patients who were on their first treatment. Specifically, patients who had been on more than one line of therapy were willing to give up only 2.2 health month equivalents (additional months of progression-free survival a new treatment would need to provide for participants to accept additional side effects) for a drug that caused increased long-term side effects, as compared to 3.7 months by patients on their first treatment.[8] These results demonstrate that patient experience is very heterogeneous and hence, should be taken into account in value assessment frameworks.

The need for capturing patient experience in value frameworks will become even more important as the concept of "comparative tolerability" enters the lung cancer space. A recent study of three PARP inhibitors in high-grade ovarian cancer demonstrated that while all three provided equivalent survival benefits, one of the inhibitors had a significantly lower toxicity profile than the other two. While the study was not designed to be a head-to-head comparison among the three drugs, it highlights the importance of quality-of-life measures (gathered through patient preference studies) in such situations where primary endpoints such as overall survival are met and may not differ dramatically across different therapies.[9] In such situations, patient preference data will be of paramount importance in determining appropriate care for a patient, where standard-of-care may evolve or multiple options exist.

3. **Use of aggregate metrics such as QALYs and evLYGs do not capture patient-level data especially in an era of precision medicine.**

The lung cancer treatment landscape has rapidly evolved over the past five years, with the Agency approving more than 15 new treatments for advanced-stage non-small cell lung cancer (NSCLC) — more than in the prior 15 years combined. Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, diagnosed in about 85% of people with lung cancer.[10,11] The complex nature of this disease requires personalized management plans for patients.[11] 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.[12-14] Now more than 20 driver mutations in adenocarcinoma have been identified — EGFR, ALK, ROS, RET, ERB2/HER2 mutations, ERB2/HER2 amplifications, MET amplifications, MET mutations, TRK, BRAF, KRAS.[15,16] 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, the first-line treatment options for EGFR and ALK positive lung cancer has changed in the last year. Furthermore, even for those NSCLC patients without a driver mutation, first-line immunotherapy with or without chemotherapy has become the standard of care.[17,18] This rapid evolution of care has increased the need to re-think patient preferences. Lung cancer patients are now living longer, higher quality lives.

QALYs or quality-adjusted life-years have long been used by economists to forecast healthcare financial decisions. While the QALY is easy to use, in their *New England Journal of Medicine,*

Neumann and colleagues point out that the QALY value typically used by healthcare economists in fact underestimates the impact of a drug.[19] In addition, QALYs are not appropriate for measuring complex health interventions (such as lung cancer treatment) where "gain of health" is not the only measure.[20] Also, QALY is an aggregate metric—it does not capture patient-level data in making economic predictions. An ideal model is one that includes patient-level metrics that can customize a prediction to an individual patient, in line with the tenets of precision medicine.

Furthermore, unlike other diseases where QALYs may have some applicability, lung cancer is not a singular disease. Rather, it is a continuum where stage of diagnosis, presence or absence of actionable mutations, recurrence, and end-of-life care would impact a patient's decision about a treatment option. Using QALYs may not adequately capture what different patients value along the lung cancer continuum.[21]

In her New York Times blog, ovarian cancer survivor Susan Gubar poignantly captures the inadequacies of QALYs in treatment decisions.[22] She writes, "[w]hatever the estimate, a crude ratio of cost effectiveness, like the QALY, seems presumptuous. How can qualitative factors (nausea, fatigue) be converted into quantitative numbers? How can general calculations account for individual variations (my preference for fatigue over nausea) or overriding personal beliefs and principles about what constitutes a valuable existence?"

We commend ICER for developing and utilizing a new metric - Equal Value of Life Years Gained (evLYG) - that evenly measures any gains in length of life, regardless of the treatment's ability to improve patients' quality of life. While evLYGs moves the focus of measurement from life extension, it continues to be an aggregate metric.

As an alternative to QALY and evLYGs, patient-reported outcomes and quality of life metrics can be used to accurately capture the differences in patient perspective along the lung cancer continuum. As pointed out by ASCO in their value framework discussion, inclusion of Patient Report Outcomes (PROs) makes their model more robust.[2] We encourage ICER to consider PROs and Quality of Life metrics, especially given that global lung cancer therapy trials now incorporate PRO measurement as a part of their study design.

4. **There is immense value in incorporating real-world data and real-world evidence about clinical practice.**

We encourage ICER to assess evidence once a drug has been used in practice for a significant amount of time to accurately capture the impact a drug has made on the survivor community. This is also related to our previous comments on PRO use in clinical trials. To be comprehensive, we recommend ICER to incorporate real-world patient experience and clinical practice data for the following reasons, given that PRO data collection is relegated to clinical trials.

1. Despite an expansion of clinical trials in global sites, an overwhelming proportion of trial participants are Caucasian (86% in 2014 vs. 92% in 1997).[23] Conducting a patient preference study within a clinical trial setting, while beneficial for submission purposes, is a missed opportunity for truly capturing the patient experience in a real-world setting, as the participant

composition does not reflect the true prevalence of the disease in a real-world setting in different racial and ethnic communities.[24]

2. Furthermore, lung cancer clinical trials often exclude patients with brain metastases and low performance status.[25] Given that a majority of advanced-stage patients present with brain metastasis at the time of diagnosis or are very sick due to the high symptom burden of lung cancer, conducting patient experience studies within a pristine clinical trial cohort does not capture the lived experience of a lung cancer patient outside of a trial setting.

As real-world data traditionally comes from four sources (clinical data from electronic health records, administrative/claims data, patient-generated/reported data, and third-party data sources through cross-industry data collaborations such as Project Data Sphere), we see ICER as being in an excellent position to develop evidentiary standards for using real-world data in value frameworks.

Conclusion

LUNGevity sincerely thanks you for the opportunity to comment on ICER's Value Assessment Framework. We look forward to additional opportunities to contribute to ICER's ongoing work and encourage the Institute to provide more opportunities for stakeholder input into its process for developing and refining its value assessment framework.

As stated, the areas of concern that we have outlined above can be actively discussed with my staff, myself, 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 encourage you and ICER to access our expertise.

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.

Thank you for your attention to this very important matter.

Sincerely,

Andrea Stern Ferris
President and Chairman
LUNGevity Foundation

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