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BONNIE J. ADDARIO
LUNG CANCER
FOUNDATION

February 14, 2017

Dr. Richard Popiel
Chief Medical Officer
Regence Blue Shield (select counties of Washington)
Regence Corporate
PO Box 1071
Portland, OR 97207

Dear Dr. Popiel:

On behalf of LUNGevity Foundation and the Bonnie J. Addario Lung Cancer Foundation, the nation's preeminent lung cancer nonprofits, that fund research, provide education and support, and build communities for the 224,390 Americans diagnosed with lung cancer each year and the over 400,000 Americans living with the disease, we appreciate the opportunity to respond to Regence Blue Shield's recent decision to not reimburse the use of pembrolizumab in the first-line setting in the treatment of advanced-stage NSCLC (Regence, 2017).

Our missions are to improve outcomes for people diagnosed with lung cancer. We have the largest lung cancer survivor networks in the country and actively engage with them to identify, understand and address unmet patient needs. We also have world class Scientific Advisory Boards (SABs) that guide the programs and initiatives of our organizations. 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.

In this era of unprecedented scientific advancements for the treatment of lung cancer, particularly in the field immunotherapy, we recognize the importance of balancing innovation with higher healthcare costs while ensuring that patients have access to life-saving therapies. However, the balance should be in favor of the patient, especially when cost-cutting strategies may deny patients with benefits of the progress we have seen in lung cancer research.

Immunotherapy was originally approved for use in melanoma, and now lung cancer is leading the research in this area – with different checkpoint inhibitors, lung cancer vaccines, and immunotherapy combinations being tested in clinical trials (Tan et al., 2016). It was a big win for the lung cancer community when the FDA approved immunotherapy options – pembrolizumab and nivolumab in 2015, and atezolizumab in 2016, all three in the second line setting – for advanced stage NSCLC (FDA, 2015a, 2015b, 2016a). It meant that our patients had more treatment options for a disease that relied on chemotherapy as the only treatment regimen.

CHICAGO OFFICE: 218 S. WABASH AVENUE, SUITE 540, CHICAGO, IL 60604 **PH:** 312.407.6100 **F:** 312.464.0737
BETHESDA OFFICE: 6917 ARLINGTON ROAD, SUITE 352, BETHESDA, MD 20814 **PH:** 240.454.3100 **F:** 240.497.0034
W: LUNGEVITY.ORG

Now, immunotherapy is an option for a subset of advanced stage NSCLC patients, in the first line setting. The FDA approved the use of pembrolizumab on the basis of rigorous clinical trial data from KEYNOTE-024 (Reck et al., 2016). The trial showed that those who received pembrolizumab had a significant improvement in progression-free survival (PFS) (HR 0.50 [95% CI: 0.37, 0.68]; p<0.001) with a median PFS of 10.3 months versus 6.0 months for those receiving platinum-based chemotherapy (FDA, 2016b). A pre-specified interim analysis demonstrated a statistically significant improvement in overall survival (OS) for patients randomized to pembrolizumab as compared with chemotherapy (HR 0.60 [95% CI: 0.41, 0.89]; p<0.005).

We were surprised to see that the Regence Medical Policy manual did not take into account findings from this important clinical trial in the decision-making process.

One of our Scientific Advisory Board members noted that "[the decision to revoke reimbursement of pembrolizumab in the first line setting] is a poorly informed decision on multiple grounds. The first-line trial of pembrolizumab vs. chemotherapy for PD-L1 positive non-small cell lung cancers was a phase III randomized controlled trial with a clear and definitive result in favor of immunotherapy. This study has been fully peer-reviewed, published in The New England Journal of Medicine, and led to an FDA approval for this therapy. Most notably, there was a clear SURVIVAL benefit for patients assigned to receive pembrolizumab, with a hazard ratio for death of 0.60 and a p value of 0.005, highly statistically significant. What is more, grade 3, 4, or 5 treatment-related adverse events occurred in TWICE as many patients on the chemotherapy group as in the pembrolizumab group (53.3% vs. 26.6%). Claiming that this therapy is "not medically necessary" is essentially stating that it is not medically necessary to offer patients treatment proven to be both more effective and less toxic. "

We also want to highlight the importance of the effect of pembrolizumab versus chemotherapy on the quality of life of lung cancer patients. The Regence policy manual states that "there is currently no evidence that it improves any clinical outcome [e.g. overall survival, symptom control, Quality of Life (QoL)] relative to standard platinum-based chemotherapy. Median OS data from this trial are not mature."

In a plenary session at the World Conference on Lung Cancer 2016 in Vienna last year, Dr. Julie Brahmer (who is also a member of our Scientific Advisory Board) presented data from KEYNOTE-024 that showed a clear improvement in the QoL of lung cancer patients who receive pembrolizumab versus chemotherapy in the first line setting (Brahmer, 2016). Her data clearly demonstrated that fewer patients in the pembrolizumab arm had deterioration in the QLQ-LC13 composite of cough, dyspnea, and chest pain (30% vs 39%), and time to deterioration was also prolonged with pembrolizumab. Dr. Brahmer concluded that pembrolizumab was associated with a clinically meaningful improvement in health-related QoL compared with platinum-based chemotherapy.

Another member of our Scientific Advisory Board who was involved in clinical trials with pembrolizumab explicitly stated "this is not a place for anecdotes, it is one for data. And we have collected enough data. I have many patients doing well years out from pembrolizumab. We have data from a randomized controlled trial indicating that survival is improved by treating the appropriate patients with frontline pembrolizumab."

As discussed above, the question of whether pembrolizumab is medically necessary has already been answered by strong scientific evidence - that pembrolizumab not only impacts overall survival, but also improves health related QoL in NSCLC patients.

The discussion outlined above can be actively discussed with our staffs, ourselves, and our Scientific Advisory Boards, 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.

We are grateful for the opportunity to comment on your reimbursement decision for the use of pembrolizumab in advanced NSCLC. Thank you for your attention to this very important matter. ***On behalf of the lung cancer community, we sincerely hope that you will reconsider your decision, and include pembrolizumab in the list of essential drugs for the first-line treatment of advanced-stage NSCLC patients***.

Sincerely,

Andrea Stern Ferris
President and Chairman
LUNGevity Foundation
aeferris@LUNGevity.org
240-454-3100

David LeDuc
Executive Director
Bonnie J. Addario Lung Cancer Foundation
dleduc@lungcancerfoundation.org
(608) 828-8844

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