Editor's Note:
The 18th World Conference of Lung Cancer (WCLC), hosted by International Association for the Study of Lung Cancer (IASLC), was held from October 15th–18th in Yokohama, Japan. It's our great pleasure to have a brief interview with Professor Heather A. Wakelee.

Meet the Professor

Professor Heather A. Wakelee: facing new progress in lung cancer research, keep in mind how do we best help patients

Submitted Oct 30, 2017. Accepted for publication Nov 07, 2017.
doi: 10.21037/tlcr.2017.11.07
View this article at: http://dx.doi.org/10.21037/tlcr.2017.11.07

Expert Introduction

Professor Heather A. Wakelee (*Figure 1*) is a Professor of Medicine at Stanford University in the Division of Oncology where she leads the thoracic medical oncology research program and has authored or co-authored over 180 medical articles on thoracic malignancies. She attended Princeton University as an undergraduate with a major in molecular biology and then went to medical school at Johns Hopkins University. She returned to her native California for internal medicine residency and fellowship training in medical oncology at Stanford University. Dr. Wakelee's focus is in clinical research in thoracic malignancies including lung cancer and thymic malignancies. She was the principal investigator of the international lung cancer intergroup trial E1505 that studied the potential role of bevacizumab in addition to adjuvant chemotherapy for resected early stage non-small cell lung cancer. Dr. Wakelee has led multiple investigator-initiated protocols and played a central role in clinical trials with bevacizumab and many other anti-angiogenic agents. Additional areas of interest include drugs and drug combinations focused on overcoming epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) inhibitor resistance, and novel immune modulatory agents. She also does population science research looking at sex differences in lung cancer, lung cancer in never-smokers and ethnic differences in lung cancer. She is the faculty director of the Stanford Cancer Clinical Trials office and is the lead investigator for ECOG-ACRIN clinical trials group at Stanford. She serves on the steering committee and is the chair of the Research Working Group of the International Thymic Malignancies Interest Group (ITMIG) and has written and conducted two phase-II trials of novel agents in this rare disease entity. She is very active in the American Society of Clinical Oncology (ASCO) and also the International Association for the Study of Lung Cancer (IASLC), for which she serves on the Board of Directors, as a Regent for the United States and on the Communications Committee.

Figure 1 Professor Heather A. Wakelee.

I was honored to meet Prof. Wakelee during the 18th World Conference on Lung Cancer (WCLC 2017) in Yokohama, Japan (*Figure 2*).

I invited Prof. Wakelee for an interview and asked her to share her expert opinions on best practices for management of EGFR-mutated non-small cell lung cancer (NSCLC) and future of check point inhibitors in lung cancer. Besides, she

Figure 2 Photo of Prof. Wakelee (middle) and AME editors.

Figure 3 Professor Heather A. Wakelee: facing new progress in lung cancer research, keep in mind how do we best help patients. Available online: https://v.qq.com/x/page/i0567o80km8.html

also shared her precious experiences on Grant application (*Figure 3*).

Interview

TLCR: With rapid development of 2nd and 3rd generation EGFR-TKIs, what's the evolving decision and best practices for management of EGFR-mutated NSCLC?

Prof. Wakelee: NSCLC patients with EGFR mutation are quite common in Asia and also in places like California where we tend to see more lung cancer in patients without a smoking history. I have a high percentage of patients with EGFR mutations in their tumors. For patients diagnosed with metastatic lung cancer, when we find that the tumor has an EGFR mutation, we know that we should start therapy with an EGFR targeted tyrosine kinase inhibitor (TKI). But, there are a lot of ways to pick which drug should be given. When we think about the availability in the US, for 1st and 2nd generation drugs, we have erlotinib, gefitinib and afatinib. And in China, there is also icotinib. We're trying to figure out which one of those is the best for an individual patient.

There are a lot of things going to make the decision, availability, cost to the patients, toxicity and then effectiveness. And between those, we don't have a lot of data to tell us one is better than another. The LUX-Lung 7 study made a comparison of gefitinib and afatinib, which proves afatinib has slightly better response rate and duration of therapy, it didn't really change the survival. So, it hasn't actually changed practice very much.

Now we have new data with the 3rd generation drug, osimertinib. The recent FLAURA study made a comparison of first-line osimertinib to gefitinib or erlotinib. In that study, osimertinib showed a clear improvement in progression free survival. This was particular noteworthy in regards to patients with brain metastases. There's a trend toward an overall survival benefit as well. So, now in the US, we have an ongoing debate on the use of osimertinib first-line and that is becoming a widely adopted strategy. But I don't think it's a straight-forward decision. I think there's still opportunity for patients to start on a 1st or 2nd generation drug and then later switch to osimertinib in some circumstances. One has to take into account a lot of different aspects. It's not just about differences in progression free survival. It's about the availability, it's about the tolerability, it's about the cost. I think all of these needed to be taken into account when we're thinking about how do we best help patients live, as well as they can, as long as they can.

TLCR: Tremendous hope is bear on immunotherapy. How do you think of the future of immunotherapy in lung cancer?

Prof. Wakelee: The checkpoint inhibitor drugs have certainly been very exciting for lung cancer treatment over the last few years. The PD-1/PD-L1 inhibitors are a category of therapy we have known about for only a few years. We know that for patients who have had first-line chemotherapy and are now in need of second-line treatment that the check point inhibitor drugs are better than single chemotherapeutic agents. However, in the patients who have EGFR mutations, which is a high percentage patients

in many parts of the world, that story is not as clear. Those patients did not have the same benefit with the checkpoint inhibitors as other patients so there's a lot we still don't understand about the check point drugs in patients with driver mutations like EGFR.

We now do have data on patients with no EGFR mutation and high expression of PD-L1 in first line therapy. The KEYNOTE-024 study compared the efficacy of pembrolizumab versus first-line chemotherapy in patients with high PD-L1 expression and no EGFR mutations or ALK translocations. The results showed that pembrolizumab provided not only a better response rate but also better overall survival. So, for patients where they are living in a country where they do have access to choose checkpoint inhibitor drugs, if they have high PD-L1 expression and they don't have an EGFR mutation or ALK translocation, pembrolizumab is a very good choice and that's something we're doing in the United States. But for patients who have EGFR mutations or other driver mutations, we start on targeted therapy and not on immunotherapy. We focus on the mutation, first then try chemotherapeutic agents, then try the checkpoint drugs with ongoing trials to help guide us.

Talking more about the checkpoint inhibitors, sometimes the checkpoint inhibitor drug treatment is successful, but sometimes it is not. These drugs are not the best approach for all patients with lung cancer but patients have high expectations. That can be a challenging discussion, as there are many patients who feel that if they don't get checkpoint inhibitor drugs, then they're somehow not getting the best possible outcome. That's not always true. So, it's important message to remember that we must balance the expectations with the reality as we continue learning more and more about how to use these drugs optimally for our patients.

Cite this article as: Zhang KP. Professor Heather A. Wakelee: facing new progress in lung cancer research, keep in mind how do we best help patients. Transl Lung Cancer Res 2017;6(Suppl 1):S108-S110. doi: 10.21037/tlcr.2017.11.07

TLCR: Grant application is essential for the scientific progress. Could you share your precious experience on it?

Prof. Wakelee: When we're talking about treatment of lung cancer, we have to think about how do we fund the research, how do we keep things moving forward, and there are a lot of different ways supporting that.

A lot of the time, there are partnerships to be able to get studies done, because it's such a big and complex process to do clinical trials. So, it's very rare that the investigators can do that on their own. There's often going to be pharmaceutical partners involved as well.

For getting grants for discovery, it's very different around the world. There's government funding, pharmaceutical company funding and enterprise funding. What we have to do is continue applying and applying and applying because it's very hard to get grants as they are very competitive. And the people who succeed are the ones who will just keep trying without giving up.

Acknowledgements

On behalf of the editorial office of *Translational Lung Cancer Research* (*TLCR*), I would like to express my gratitude to Prof. Wakelee for sharing her opinions with us. I would also like to thank my colleague, Grace Li, for her assistance of the interview.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

(Science Editor: Kaiping Zhang, TLCR, tlcr@amepc.org)

