Professor Caicun Zhou: a successful step forward for international exchange on combating lung cancer

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Prof. Caicun Zhou (*Figure 1*), PhD, MD, is director of the Department of Oncology, Shanghai Pulmonary Hospital, director of Cancer Institute of Tongji University Medical School, chairman of the Oncology Department of Tongji University. He studied in Japan for 2 years and was a visiting scientist in USA for half a year. Prof. Zhou is a committee member of the Chinese Association of Lung Cancer and the Chinese Society of Clinical Oncology, and is a council member of the Shanghai Anti-Cancer Association, the Shanghai Pneumonology Association, and the Shanghai Oncology Association. Prof. Zhou is the Co-Editor-in-Chief of *Translational Lung Cancer Research*. He also serves as a member on the editorial boards of many other scientific journals, including '*Tumor*', '*Chinese-German Journal of Clinical Oncology*', '*China Oncology*' and the '*Chinese Journal of Clinical Oncology*' and also associate editor of *Lung Cancer*. Prof. Zhou was selected as an 'excellent learning pioneer' by the Science and Technology Commission of Shanghai Municipality (STCSM) in 2006, and got grants from the National 863 project and five other key research projects of the STCSM. His major research interests are in customized and targeted therapy of lung cancer, and he has published over 100 papers in scientific journals.

On the 14th Central European Lung Cancer Congress held in Vienna in Dec 2014, Prof. Zhou as the faculty member of the Chinese-Central European Symposium, together with other invited Chinese experts, gave important speeches to introduce lung cancer's epidemiology, primary prevention, treatment of lung cancer, and the ongoing trials in China to the European fellows. Though this congress has closed, the scientific contents conveyed on the congress remain valuable. And it also has set up a successful example of effective exchange between China's and Central European's researchers and clinicians in the field of lung cancer. Hope this interview (*Figure 2*) will bring you some insights unexpected.

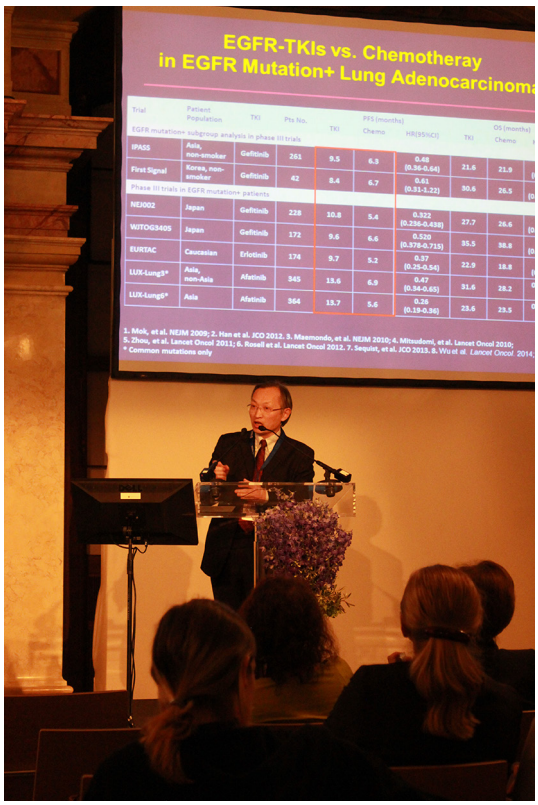

Figure 1 Professor Zhou was giving his speech on the 14th Central European Lung Cancer Congress.

TLCR: You have given an important speech about epidermal growth factor receptor (EGFR) on the congress. Would you like to summarize your speech to share with those who did not attend this congress?

Prof. Zhou: Actually, I gave a talk on the treatment for the patient of positive EGFR mutation. Now we know that the patients with positive EGFR mutation survive much longer if they are treated with EGFR tyrosine kinase

Figure 2 Professor Zhou was speaking at the interview.

inhibitors. Adenocarcinoma with positive EGFR mutation depends upon EGFR signaling pathway and inhibition of the pathway will lead to apoptosis of cancer cells. So up to now, we have several trials comparing first-line EGFR tyrosine kinase inhibitors (including gefitinib, erlotinib as well as afatinib) verses chemotherapy in the first-line treatment of the advanced non-small cell lung cancer with mutant EGFR. EGFR tyrosine kinase inhibitors do better than chemotherapy in terms of progression-free survival, tumor response rate and quality of life, but there is no study to show survival benefits. Why? Some audience questioned why clear progression-free survival benefit did not translate into survival benefit in these trials. There may be several reasons for this question, including small sample-sized study, which is underpowered to show survival benefit, overall survival being not primary endpoint, and also post-study crossover therapy. LUX-Lung 3 and LUX-Lung 6 are aimed to compare afatinib versus standard chemotherapy in patients with positive EGFR mutation. These two trials have several similarities: the same population, the same experimental arm on afatinib, the same design and the same primary endpoint, thus giving us a kind of opportunity to make pooled-analysis of two trials. When we did, we found clear survival benefits with afatinib versus chemotherapy in the population with positive common EGFR mutation. When we look at different EGFR mutations, the survival benefit is quite clear in those with exon 19 deletions, but not in those with exon 21 point mutation. When we looked at other efficacy parameters, afatinib did better than chemotherapy in terms of tumor response rate and PFS and patients with EGFR exon 19 deletions could get even more clinical benefits from afatinib. Adenocarcinoma with EGFR exon 19 deletions and exon 21 point mutation are not twins but are brothers. Nowadays, we can treat them together with first-line EGFR inhibitors as standard therapy.

TLCR: Is there any pending question still needing further exploration after your study on EGFR tyrosine kinase inhibitors that you presented above?

Prof. Zhou: Actually, there is only one pooled study analysis to show survival benefit with EGFR tyrosine kinase inhibitor, afatinib. Other studies didn't find any survival benefit. So there is a question—why the survival benefit is clear with afatinib, but not clear with other EGFR tyrosine kinase inhibitors, such as gefitinib or erlotinib? The survival benefit is due to a compound with afatinib or happens by chance? This question is difficult to answer. It may be due to the chance. These studies are comparatively small, but we do find that the survival benefit in patient with exon 19 deletions is consistent between two trials LUX-Lung 3 and LUX-Lung 6. Maybe it is due to the compound, as afatinib is the second-generation of EGFR tyrosine kinase inhibitor.

TLCR: The Chinese-Central European Symposium on this congress actually provided a bridge for the researchers between China and Central Europe to exchange their studies on lung cancer. As you are the faculty member of this symposium, what have Chinese speakers mainly introduced to the European audiences?

Prof. Zhou: It is the first joint symposium between Chinese doctors and Central European doctors. We have four speakers whose talks were focused on lung cancer's epidemiology, primary prevention, the treatment of the advanced stage lung cancer, and the ongoing trials in China. So they gave the European audiences a kind of introduction to lung cancer in China. As you know, lung cancer incidence is still increasing in China. It is increasing in females as well as in males. The reason for the increasing incidence of lung cancer may be due to high prevalence of smoking, out-door pollution, indoor pollution and so on. Mortality of lung cancer in China is top one. In China, we find a large number of never-smokers with lung cancer. The molecular and clinical features of lung cancer between the smoking and the non-smoking patients are different. We find higher stage-IV disease in never-smoking patients with lung cancer, higher proportion of adenocarcinoma in never-smoking patients, and also higher incidence of EGFR mutation in never-smoking patients. As to histology,

we found adenocarcinoma become the largest subtype of lung cancer. We also observe decreasing incidence of the squamous-cell carcinoma in the past 10 years. So the adenocarcinoma incidence becomes the top One and that of squamous-cell carcinoma becomes top two among lung cancer subtypes. Dr. Xiuyi Zhi gave a short introduction on the primary prevention of lung cancer in China. Dr. Jie Wang gave us an introduction of treatment for advanced non-small cell lung cancer. She focused on two things. One is about patients without oncogenic drivers. If patients are found with EGFR mutation, EGFR tyrosine kinase inhibitors are recommended according to our guidelines. If patients are found with anaplastic lymphoma kinase (ALK) translocation, crizotinib is recommended. Detection rate for EGFR and ALK is not so high according to the survey about 2 years ago, which was published on the Journal *Lung Cancer*. Only about 18% of patients were tested in that survey. But nowadays, I think the testing rate is going up. In our center, over 60% of patients in advanced stage are tested for EGFR and ALK. For those without oncogenic drivers, the most common used first-line chemotherapy is cisplatin-gemcitabine or carboplatin-gemcitabine, followed by cisplatin or carboplatin-docetaxel. Only about 50% of our patients received second-line therapy. The most common used second-line agents include docetaxel and EGFR tyrosine kinase inhibitors. I think that is the main content that Dr. Wang gave during the meeting. As to the next topic presented by Prof. Yilong Wu, he gave us a short introduction of the ongoing Phase III trials. He gave a talk on the biomarker-driven studies, such as study on the EGFR mutant non-small cell lung cancer, and we have OPTIMAL, ENSURE, IPASS, LUX-Lung 6. For patients with positive ALK, we have several trials ongoing. He also gave us some kind of introduction on the trials on adjuvant therapy, including his trial comparing adjuvant and neoadjuvant chemotherapy in Stage II and III non-small cell lung cancer with chemotherapy regimens of the docetaxel and carboplatin. He also introduces his adjuvant trial on EGFR tyrosine kinase inhibitor. The trial finished recruitment a few months ago and we are waiting for the results.

TLCR: Have you got some insights after the exchange with the European fellows on the Chinese-Central European Symposium?

Prof. Zhou: We just talked on smoking cessation. Maybe it is a good point that we can work together on the smoking cessation. In this session, Dr. Jacek Jassem from Poland gave us a good introduction of the smoking cessation in Poland. After their efforts, the smoking prevalence has been decreased greatly, which is needed to decrease the incidence of lung cancer in Poland. So these strategies to ban smoking are kind of successful in some sense. So I think their strategies are very helpful to China to control smoking. It is kind of good experience for us. At present, different areas could cooperate together on screening lung cancer. From the symposium, we can see that they have a kind of cooperation in the screening of lung cancer in the Central European countries. For the methods of screening lung cancer, we can use the low-dose computed tomography (CT). But as you know, the majority of the nodules found by the CT scan are not malignant. Therefore, maybe we can work together to differentiate the malignant and benign lung nodules. This is very helpful to us.

TLCR: Thank you very much!

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None.

Footnote

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

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