

Dr Haiquan Chen: clinical significance of RET fusion gene for patients with NSCLC

Zhijia Feng

DXY Website, Guanlan Networks (Hangzhou) Co. Ltd., Binjiang District, Hangzhou, China

Corresponding to: Zhijia Feng. DXY Website, Guanlan Networks (Hangzhou) Co. Ltd., 3/F, Building 1, Lesu Sci-Tech. Park, 1526 Chunbo Road, Binjiang District, Hangzhou, China. Email: riset@dxyer.com.



Submitted Nov 10, 2012. Accepted for publication Dec 13, 2012.

DOI: 10.3978/j.issn.2218-6751.2012.12.02

Scan to your mobile device or view this article at: <http://www.tlcr.org/article/view/835/1418>

Recent researches found RET fusion gene, exists in part of the NSCLC subgroup. Due to limited knowledge in this kind of oncology, a study aiming to determine the clinicopathologic characteristics of the RET fusion gene in NSCLC patient was carried out by experts such as Dr Rui Wang and Dr Haiquan Chen from Fudan University Cancer Center in Shanghai. The study was published in *Journal of Clinical Oncology* (Nov. 13, 2012).

In the study, a total of 963 patients with NSCLC who received resection as treatment were examined through RT-PCR coupled with real time quantitative PCR. The result was tested by immunohistochemistry and fluorescence in situ hybridization (FISH). Meanwhile, a subset of 633 lung adenocarcinomas was also studied for EGFR, KRAS, HER2, and BRAF mutations, as well as ALK rearrangements. The patient characteristics were also collected such as age, gender, history of smoking, staging and grade of tumor, categorization of subtype of lung adenocarcinoma by International Society of Lung Cancer Research, American Thoracic Society or European Respiratory Society, and patients' progression-free survival (PFS).

Among the 936 patients with NSCLC, 13 were found to have RET fusion gene (11 out of 633 patients with adenocarcinoma, 2 out of 24 patients with adenosquamous carcinoma). Of the 13 patients with fusion gene, 9 was found to have KIF5B-RET, 3 have CCDC6-RET, 1 have NCOA4-RET, a lately discovered fusion gene. Patients with RET fusion gene manifest a poor differentiation of tumor cell (63.6%; $P=0.029$ for RET *vs.* ALK, $P=0.007$ for RET *vs.* EGFR) with a tendency to be younger (≤ 60 years; 72.7%) and never-smokers (81.8%), to have solid subtype (63.6%) and a smaller tumor (≤ 3 cm) with N2 disease (54.4%). The median relapse-free survival was 20.9 months.

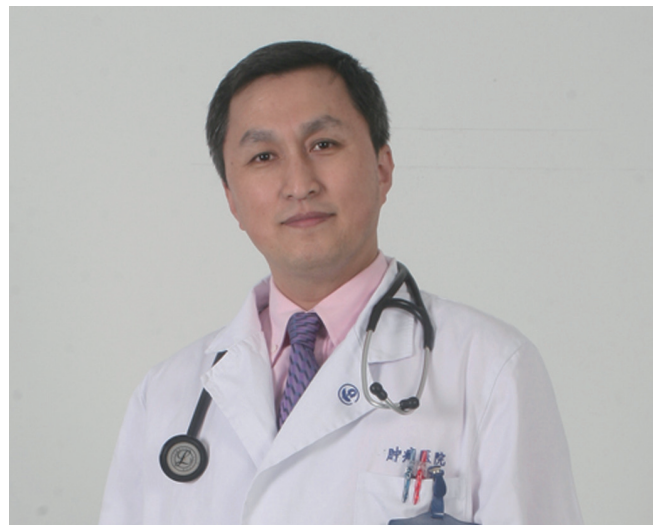


Figure 1 A snapshot of Dr Haiquan Chen

Researchers such as Dr Rui Wang believed that the result that 1.4% of patients with NSCLC and 1.7% of patients with lung adenocarcinoma have RET fusion gene with identifiable clinicopathologic characteristics, warrants RET fusion gene's role in clinical consideration and targeted therapy research (1).

We are honored to have an interview with Dr Haiquan Chen (Figure 1), one of the researchers and author of this study. This interview was carried out and published soon after the study appears online.

DXY: Patients involved in the study are mostly Chinese. Is the distribution of RET fusion genes of East Asians and Caucasians different from that of Chinese?

Prof. Chen: Pasi A. Janne *et al.* have done the comparative

study of the distribution of RET fusion gene in Chinese and Caucasian population and found that the incidences of RET fusion genes are closed with about 2%, also mainly among never-smoker, smaller-tumor Pulmonary adenocarcinoma patients. However, study of the other clinical pathological features in Caucasian RET fusion genes patients has not been carried out by Pasi A. Janne *et al.* which need to be investigated more.

DXY: It was mentioned in the paper that of the 13 patients who are detected with exclusive RET fusion gene, the differentiated tumors are low. Does different type of RET fusions affect tumor differentiation?

Prof. Chen: We found three types of RET fusions, KIF5B-RET, CCDC6-RET and NCOA4-RET. KIF5B-RET and CCDC6-RET are not significantly different from each other with rather low differentiations. NCOA4-RET were only found in one patient that we cannot tell if it is the same with the other two types with low quantity of cases.

DXY: What targeted drugs can be used to treat RET fusion genes NSCLC patients? What's your study's impact on clinical application and the targeting therapy of Lung Cancer?

Prof. Chen: Vandetanib, Sorafenib and Sunitinib are the three targeted drugs use to inhibit the activity of several receptor tyrosine kinase (RTK) including RET and damage the RET fusion gene cell. Besides the features of younger (≤ 60 years old), never-smokers, with mediastinal lymph node metastasis despite the entity subtype and smaller tumor, our study also put forward a fast and accurate method to detect the fusion genes which give support in selecting RET fusion genes patients, and RET positive NSCLC clinical trials of Tyrosine Kinase Inhibitors targeting in RET.

DXY: Currently, diagnosis and treatment of cancer, especially the NSCLC have evolved from pathologic diagnosis to molecular subtype diagnosis. What challenge do you think that Chinese clinical doctors would face?

Prof. Chen: In recent years, the survival rate of tumor cells of NSCLC, especially the adenocarcinoma of lung depends on a certain key oncogene, which is call oncogene addiction. By the weakness of the tumor cell, we can develop a targeting drug that selectively inhibite or shut down the activity of the gene and then damage the tumor. It is a therapy strategy that has achieved great success. The therapy is to devide the Lung Cancer to several molecular subtypes and to treat with the relative molecular targeted drugs independently. Currently, 90% of the East Asian never-smoker adenocarcinoma of lung patients have the known oncogenes most of whom would take a matching targeting therapy. Since more than 10 key oncogenes have been discovered, it would be the first challenge for clinical doctors to establish a reasonable selective strategy to detect the oncogenes group and to carry out a matching targeted therapy. Iressa and Tarceva to EGFR and Crizotinib to ALK have become the first-line targeted drug for oncogenes-carrying patients, while drug for other targets are still in the clinical trial level. And those drugs still need Chinese Clinical doctors to design the clinical trial to approve their effects. Finally, although the new targeted drugs extend the overall survival of the patients, most patients suffer from the drug resistant, leading to the failure of the treatment.

It will be a tough challenge for every clinical doctor to study the Resistant Mechanism of the targeting agents and to figure out the best treatment to overcome the resistance.

Acknowledgements

Disclosure: The author declares no conflict of interest.

References

1. Wang R, Hu H, Pan Y, et al. RET Fusions Define a Unique Molecular and Clinicopathologic Subtype of Non-Small-Cell Lung Cancer. *J Clin Oncol* 2012;30:4352-9.

Cite this article as: Feng Z. Dr Haiquan Chen: clinical significance of RET fusion gene for patients with NSCLC. *Transl Lung Cancer Res* 2013;2(1):E23-E24. DOI: 10.3978/j.issn.2218-6751.2012.12.02