

# 비소세포폐암의 최신 경향

안명주

성균관대학교 삼성서울병원 혈액종양내과

## Recent Progress in Non-Small Cell Lung Cancer: Prime Time for Personalized Therapy

Myung-Ju Ahn

Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Lung cancer remains the leading cause of cancer death worldwide and non-small-cell lung cancer (NSCLC) accounts for 80% of lung cancer. During the last several decades, tremendous progress in understanding lung cancer biology and development of technology has been achieved, leading to improvement in screening, diagnosis, molecular biology, and management including chemotherapy, targeted therapy and radiotherapy. In this issue, each part of NSCLC field will be discussed by several experts.

During 1980's, only K-ras mutation has been known to be involved in the development of NSCLC. Since EGFR mutation, the landmark biomarker was found in 2004, substantial development in understanding of molecular biology of lung cancer has been achieved especially in adenocarcinoma of lung and even in squamous cell carcinoma recently. Identification of EGFR mutation and development of its targeted agent, EGFR tyrosine kinase inhibitor has shed light on personalized therapy in NSCLC, in which oncogenic addiction has been proved to exist even in solid tumors. Choi will extensively review the molecular biology of NSCLC including several oncogenes (EGFR, K-ras, ALK, RET, ROS1, and FGFR1), tumor suppressor genes (p53, CDK/p16/RB, and LKB1), angiogenesis, epigenetics, microRNA, telomere/telomerase, and cancer stem cells [1]. Accordingly, the importance of detection of

these genotypes for personalized therapy and also many unresolved issues regarding new technologies, including next generation sequencing will be discussed.

NSCLC has been considered one disease along with small cell lung cancer, because several histologically defined subtypes, adenocarcinoma, squamous cell, and large cell carcinoma did not affect the prognosis or management of NSCLC long time before. However, cumulative studies demonstrating the different outcomes for specific chemotherapy or targeted agents according to the underlying histology subtype emphasized the importance of pathology. Moreover, the growing evidences that lung cancer is heterogeneous and composed of many small molecular subsets according to molecular genotyping, followed by significant improvement of clinical outcomes to specific targeted agents demonstrate the importance of biomarkers along with accurate histological diagnosis of NSCLC. Therefore, aspiration cytology for diagnosis of lung cancer is not acceptable anymore, and large amount of tissue acquisition as much as possible became the critical issue for accurate diagnosis along with molecular genotyping. Jung will discuss in detail the importance of histology in NSCLC and how several molecular tests should be performed efficiently with small biopsy specimen for making treatment decision [2].

Correspondence to: Myung-Ju Ahn

우-135-710, 서울시 강남구 일원로 81, 삼성서울병원 혈액종양내과

Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, 81 Irwon-ro, Gangnam-gu, Seoul 135-710, Korea

Tel: +82-2-3410-3438, Fax: +82-2-3410-1754, E-mail: silkahn@skku.edu

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Most of NSCLC patients are diagnosed at an advanced stage due to no adequate tool for early detection available despite extensively performed screening programs, leading to high mortality. Recently, low-dose computed tomography (LDCT) has emerged as a promising method for early detection from well-designed randomized trial. Won will review many trials which were conducted for lung cancer screening and also the limitations and possible application of LDCT as screening method for NSCLC [3].

Staging is critical for making treatment decision especially in NSCLC. Mediastinoscopy has been considered gold standard for staging of mediastinum, but it is invasive and requires general anesthesia. As a non-invasive technique, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) or endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) has emerged as a new diagnostic modality which allows not only high sensitivity and specificity for mediastinal staging but obtaining adequate biopsy for molecular genotyping. The advantages and limitations of EBUS will be discussed by Um [4].

Surgical resection is the primary treatment modality for early-stage NSCLC. Along with other field of cancer surgery, minimal invasive surgery such as video-assisted thoracic surgery (VATS) has been extensively studied and adopted rapidly in the management of early stage NSCLC. Cho et al will discuss in detail on the VATS regarding techniques, clinical outcomes, and future directions [5].

Almost all patients with NSCLC except very early stage need chemotherapy in some point of disease process. These include adjuvant, neoadjuvant chemo- or chemoradiotherapy, definitive concurrent chemoradiotherapy or palliative chemotherapy. Platinum doublets did improve overall survival in metastatic NSCLC, but no difference of clinical outcomes was noted among different types of regimen. Recently, maintenance therapy either continuous or switch has improved progress free survival and overall survival in part. Park will extensively review the current issues of chemotherapy in NSCLC [6].

With advances in molecular biology of lung cancer and technology, many genomic abnormalities have been known to be involved in lung cancer, leading to the development of agents which can specifically target those abnormalities. EGFR TKI is the first targeted agent which demonstrated significant improvement of clinical outcomes in activating EGFR mutant NSCLC, resulting in paradigm shift of treatment of NSCLC to personalized therapy. The identification of EML4-ALK and development of ALK inhibitor further

led to rapid progress. Many compounds targeting ROS1, RET, B-raf, FGFR1, c-met, or others have been developed and actively involved in clinical trials. Along with these agents, the importance of identification of biomarker has been emphasized ever than before, although no promising biomarker for angiogenic inhibitors is available so far. In addition to the targeted agents, immunotherapy such as immune check point inhibitors is emerging new approach to treat NSCLC. Ahn will discuss the updates of current targeted agents in NSCLC [7].

Radiotherapy has been used for the treatment of NSCLC for a long time and still remains one of the main treatment modalities together with surgery and systemic chemotherapy. During the last decades, significant progress has been made in the techniques of radiotherapy. Recently, stereotactic ablative radiation therapy (SABR) became the emerging new technique, in which it can deliver high dose of radiation with very small target volume, resulting in low incidence of side effects with comparable clinical outcomes to surgery in early stage NSCLC patients who are inoperable or medically unsuitable for surgery. Ahn will discuss the current status of SABR in NSCLC [8].

Although advances in one specialty area of lung cancer research informed advances in other areas as well and lots of progress has been achieved in NSCLC, we still have a long way to go. Given the complexity of NSCLC, multidisciplinary team approach including biology, molecular biology, epidemiology, pathology, pulmonology, medical oncology, thoracic surgery, radiation oncology, public health and supportive care should be needed to combat this dreaded disease.

## REFERENCES

1. Choi JH. Molecular biology of non-small-cell lung cancer. *Hanyang Med Rev* 2014;34:4-9.
2. Chung JH. Current issues in lung cancer pathology. *Hanyang Med Rev* 2014;34:10-4.
3. Won YW. Lung cancer screening. *Hanyang Med Rev* 2014;34:15-9.
4. Um SW. The role of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in the diagnosis and staging of lung cancer. *Hanyang Med Rev* 2014;34:20-5.
5. Cho JH, Choi YS. Minimally invasive thoracic surgery in lung cancer operation. *Hanyang Med Rev* 2014;34:26-30.
6. Park BB. Chemotherapy for non-small cell lung cancer. *Hanyang Med Rev* 2014;34:31-6.
7. Ahn MJ. Molecular targeted therapy in lung cancer. *Hanyang Med Rev* 2014;34:37-44.
8. Ahn YC. Role of radiation therapy for non-small cell lung cancer: focused on stereotactic ablative radiation therapy in early stage. *Hanyang Med Rev* 2014;34:45-50.