Basic Treatment Strategies for Lung Cancer

JMAJ 46(12): 532–536, 2003

Akira INOUE* and Nagahiro SAIJO**

*Respiratory Oncology and Molecular Medicine, Institute of Development, Aging, and Cancer, Tohoku University
**Division of Internal Medicine, National Cancer Center Hospital, Tokyo

Abstract: Lung cancer is the leading cause of death from malignant diseases in Japan. Treatment of lung cancer should be selected appropriately according to clinical staging based on scientific evidence. Small cell lung cancer should be managed mainly with platinum-based chemotherapy, and the concurrent use of chemotherapy and radiotherapy is recommended for limited disease. Non-small cell lung cancer should be managed mainly by surgery for stage I and stage II, combined chemo-radiotherapy for stage III, and chemotherapy for stage IV. Chemotherapy is also suggested to be effective in relapsed cancer. The efficacy of these therapies has only been demonstrated in patients with favorable performance status (PS). Treatment lacking sufficient evidence of benefit should not be given to patients with poor PS. The use of newly developed agents, such as gefitinib and other molecular target drugs, must be considered cautiously in terms of applicability to individual patients. The development of better treatment methods needs to be based on evidence from clinical trials.

Key words: Lung cancer; Chemotherapy; Performance status; Evidence-based medicine

Introduction

Lung cancer is the leading cause of death from malignant diseases in Japan. Predictions indicate further increase in the prevalence of this disease. Clinicians have many opportunities to come in contact with patients with lung cancer, starting from the first visit of a patient presenting coughs and other symptoms to the process of definitive diagnosis and treatment.

This paper discusses the basic treatment strategies for lung cancer. Please refer to other articles for detailed information concerning the treatment of various forms of lung cancer.

From the First Examination to Staging

Patients with lung cancer often present at a hospital complaining of nonspecific symptoms such as coughing, and are found to have abnormal shadows on chest X-ray. Care should be taken in the interpretation of chest X-ray
images not to overlook lesions in the areas overlapping the shadows of the heart, blood vessels, and bones, as well as old tuberculosis foci.

In the next step, thoracic CT should be performed to obtain more detailed information. In this case, use of a contrasting agent is recommended to facilitate the detection of mediastinal lymph node metastasis.

Once the location of lesions in the lungs has been identified, tumor tissues for histopathological examination are sampled using bronchoscopy, CT-guided biopsy, or other means. It should be noted that sputum cytology might provide a low-invasive method of diagnosis particularly suited to patients showing poor performance status (PS).

Understanding the PS of the patient is important in examining a patient with lung cancer. Because active treatment such as surgery and chemotherapy with antineoplastic agents places great physical and psychological burdens on the patient, such treatment for the patients with poor PS has to be often abandoned. If the patient presents problems requiring urgent action (e.g., severe pain, dyspnea due to tracheal stenosis, and neurological complications due to brain metastasis), symptomatic treatment for such problems should be given priority.

**Selection of Appropriate Therapies According to Clinical Staging**

Once the histopathological diagnosis of lung cancer has been established, detailed whole-body examinations (e.g., brain MRI, abdominal CT or abdominal echo, and bone scintigraphy) should be performed promptly to investigate possible distant metastases. Therapies are selected according to histopatho-
logical typing) and clinical staging (TNM classification) as summarized below (see flow chart in Fig. 1).

1. **Treatment of small cell lung cancer**
   Because small cell lung cancer is characterized by rapid progression and the propensity for distant metastasis, surgery is recommended only in the very early stage of the disease (stage I). On the other hand, chemotherapy and radiotherapy are important treatment for small cell lung cancer, because it responds to these therapies. Combined use of chemotherapy with cisplatin plus etoposide (PE) and radiotherapy is reported effective when the tumor is localized within the field of irradiation (limited disease; LD). Addition of prophylactic cranial irradiation is recommended for patients showing complete remission on imaging diagnosis.

   However, small cell lung cancer showing systemic progression (extensive disease; ED) can be managed only by chemotherapy (although radiotherapy may be used to alleviate symptoms). While PE therapy has been the standard treatment for a long time, a comparative study conducted recently by the Japan Clinical Oncology Group (JCOG) suggested that the combination of cisplatin and irinotecan might be superior to PE therapy.

2. **Treatment of non-small cell lung cancer**
   Treatment of non-small cell lung cancer must be selected carefully according to different stages of the disease: cure by surgical treatment is expected in stages I and II; so-called multidisciplinary therapy consisting of combined chemo-radiotherapy with or without surgery is effective in stage III; and chemotherapy is used for elongation of survival in stage IV, where curative treatment is difficult.

   The results of several clinical studies have suggested that resectable stage III cases benefit from preoperative chemotherapy. However, no consensus has been reached as to the type of appropriate antineoplastic agents and the propriety of the concurrent use of radiotherapy. These problems need to be clarified by clinical trials, and this will require collaboration among internal medicine, surgery, and radiology departments. See ASCO (American Society of Clinical Oncology) guidelines for information concerning the treatment of unresectable non-small cell lung cancer.

   A recent trend in the chemotherapy for advanced non-small cell lung cancer is the reports of efficacy of several regimens combining newly developed antineoplastic agents and platinum-based antineoplastic agents. Although combinations of new antineoplastic agents (so-called non-platinum regimens) have been reported effective, evaluation of such regimens is still considered insufficient at present. We should be cautious about the use of combinations of new drugs.

3. **Treatment for relapsed or refractory lung cancer**
   Both the patients with small cell lung cancer and non-small cell lung cancer are followed up at approximately monthly intervals. If progression of the tumor is observed after (or during) treatment, secondary treatment is indicated for patients having good PS. Relapsed small cell lung cancer is treated with several regimens such as CODE therapy (chemotherapy with cisplatin, vincristine, doxorubicin, and etoposide), but no standard treatment has been established. This needs to be addressed in future study.

   Docetaxel is reported effective in the treatment of relapsed non-small cell lung cancer. Gefitinib (Iressa), a new agent developed simultaneously in Japan and Europe, is showing successful results as a second-line treatment for non-small cell lung cancer patients who have been treated with platinum-based agents.

4. **Treatment for patients with poor PS**
   As discussed above, active treatment may increase the risk of worsening the prognosis of patients with poor PS. Pain relief and other symptomatic treatments are usually considered
the best strategy for these patients (although chemotherapy may be attempted for untreated small cell lung cancer even in patients with poor PS, because such tumors often respond to chemotherapy).

The patients and their families may not be satisfied with the strategy of “doing nothing (against the cancer itself),” but the physicians should refrain from sharing such sentiment and discontinue treatment lacking scientific evidence and medical meaning (such as a chemotherapy regimen using aimlessly reduced doses).

Aimless administration of oral antineoplastic agents after surgery is unsupported by scientific evidence.15) With these problems in mind, we should be very discreet in using oral antineoplastic agents, including gefitinib and other new additions to our arsenal.16)

**Conclusion**

This paper outlines the basic strategies for lung cancer treatment.

Because the number of specialized oncologists is still small in Japan, generalist clinicians are engaged in the treatment of lung cancer, and many patients are receiving benefit from their services. In determining treatment strategies, physicians should sufficiently understand contemporary criterion standards and practice evidence-based medicine. Because no single method of therapy is sufficiently effective to ensure the success of lung cancer treatment, it is important to promote the development of better therapies through clinical trials and the collaboration between specialized cancer hospitals and community-based hospitals.

**REFERENCES**


2) National Cancer Institute: Cancer Information (on the Internet).


14) Fukuoka, M., Yano, S., Giaccone, G. et al.: Final results from a phase II trial of ZD1839 (‘Iressa’) for patients with advanced non-small-cell lung cancer (IDEAL 1). *Proc Am