Short Review

Developments in the Treatment of Non-small Cell Lung Cancer

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Abstract. *Lung cancer remains the leading cause of cancer-related deaths among men and women in the civilized world. Although there have been major improvements over the recent decades in surgical techniques and the role of chemotherapy-radiotherapy in the treatment of non-small cell lung cancer (NSCLC), the long-term outlook for these patients has not changed significantly. The median survival for patients with advanced-stage NSCLC treated with platinum-based chemotherapy is a disappointing 8-10 months. In current clinical practice, chemotherapy is used as a combined modality with radiotherapy as an adjuvant or neoadjuvant therapy. Moreover, combination chemotherapy is regarded as the standard care in the treatment of unresectable locally advanced (stage IIIb), metastatic (stage IV), or recurrent disease. The recent developments in the treatment of NSCLC have been focused on the emerging role of adjuvant therapy in the early stages of NSCLC. The clinical activity of pemetrexed, a multi-targeted antifolate anticancer agent, as a second-line chemotherapy agent and the impact of new biological agents, such as bevacizumab and erlotinib, have been investigated in phase III trials in the first- and second-line setting. Even though these options have been available in the last few years, there is a clear need for improvement in the current standard of care. No definite survival benefit has yet been demonstrated. An abundant amount of research is still required in the field of lung cancer therapy with well-designed clinical trials and appropriate patient selection.*

There are multiple levels of approaching lung cancer management in our medical scientific society, such as thoracic surgery for early stages of NSCLC, chemoradiation therapy of locally advanced NSCLC or systemic chemotherapy of metastatic NSCLC. It was estimated in the United States that in 2007 there will be approximately 174,000 new diagnoses of lung cancer from which 162,000 deaths would result (1).

Regardless of the cancerous cell origin, prognosis is uniformly dismal in any advanced disease, even though 80% of lung cancer cases are of the non-small cell type and the primary therapy is systemic chemotherapy. Moreover, the 5-year survival for lung cancer has remained at <15% for the past 20 years (2). Given the above data, it is realized that a number of therapeutic strategies have to be investigated to improve the overall survival, symptoms and quality of life of lung cancer patients.

The recent developments in the treatment of NSCLC have been focused on the emerging role of adjuvant therapy in the early stages of NSCLC. The clinical activity of pemetrexed, a multi-targeted antifolate anticancer agent, as a second-line chemotherapy agent and the impact of new biological agents, such as bevacizumab and erlotinib have been investigated in phase III trials in the first- and second-line setting.

Adjuvant Chemotherapy

In 1995, the Non-Small Cell Lung Cancer Collaborative Group published a meta-analysis that evaluated the role of cisplatin-containing regimens in all stages of this disease. It included 14 randomized trials of surgery with or without adjuvant chemotherapy in NSCLC; eight of these studies employed cisplatin-based regimens. In this analysis of 1394 patients, there was a 5% improvement in overall survival at 5 years which did not reach statistical significance. In addition, there was also a 13% reduction in the risk of death, which was borderline to statistical significance, using cisplatin-based adjuvant chemotherapy compared with those on observation alone (3). This led to the planning and execution of multiple national and international trials that were adequately powered to look for this 5% improvement in overall survival at 5 years.

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