State of the Art of Non-Small-Cell Lung Cancer in the New Millennium

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Lung cancer is the leading cause of cancer death worldwide, with mortality rates in most developed countries ranging from 35 to 95 fatalities per 100,000 in men and 10 to 20 deaths per 100,000 in women.[1] Non-small-cell lung cancer is the most common lung malignancy, accounting for more than 75% of all lung cancers. At time of diagnosis, approximately 60% of non-small-cell lung cancer cases are locally advanced or metastatic, and more than 85% of patients diagnosed with this neoplasm die of their disease. The 5-year survival of patients presenting with locally advanced disease is about 10%, and for those with stage IV disease, survival drops to 1%.[2] These dismal outcomes have not changed over the past 2 decades, and thus the need for more effective treatment is obvious.

During the past 20 years, clinical investigators have attempted to develop chemotherapeutic regimens that effectively prolong survival and provide palliation for patients with non-small-cell lung cancer. Recent meta-analyses have shown that platinum-based chemotherapy combined with thoracic radiotherapy (TRT) improved survival in the setting of locally advanced non-small-cell lung cancer, as compared with radiotherapy alone. Combinations of platinum and TRT increased median survival by 3 months and demonstrated a 5% increase in 5-year survival.[3] Furthermore, data from randomized trials of concurrent chemoradiation in unresectable stage III non-small-cell lung cancer have indicated significant improvements in survival, and several ongoing single-arm phase I/II trials assessing new agents in combination with TRT have shown encouraging results.

In the late 1990s, several new agents emerged from clinical development and demonstrated activity against non-small-cell lung cancer, including gemcitabine (Gemzar), paclitaxel (Taxol), docetaxel (Taxotere), vinorelbine (Navelbine), and irinotecan (CPT-11, Camptosar). In a 1998 article, Bunn and Kelly[4] reviewed phase II studies of these new agents and listed single-agent objective responses of ≥ 20% (range: 13%-27%), with median survival duration of about 40 weeks (range: 34 to 38 weeks), and 1-year survival of 40% (range: 24% to 52%) (Table 1). When these agents were evaluated in combination with platinum compounds, the overall response rates ranged from 35% to 47% with a median survival of 34 to 57 weeks; average 1-year survival ranged from 35% to 61% (Table 2).

In addition, a number of novel targeting therapies are under investigation in non-small-cell lung cancer, including matrix metalloproteinase inhibitors, epidermal growth factor inhibitors, vascular endothelial growth inhibitors, farnesyl transferase inhibitors, cyclin dependent kinase inhibitors, and gene therapy (Table 3). However, at present, it is reasonable to consider that the newer chemotherapy agents used in combination with a platinum compound are the most effective regimens in patients with advanced non-small-cell lung cancer. Of these recently approved agents, gemcitabine has provoked considerable interest, and it is the purpose of this symposium to clarify gemcitabine’s role in the treatment of non-small-cell lung cancer.

References:


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