Chapter Overview

In the past decade, chemotherapy has been firmly established as a relevant treatment strategy for patients with advanced non–small cell lung cancer (NSCLC) and good performance status. In the 1990s, existing platinum-based regimens were shown to double 1-year survival rates, to approximately 20%, as compared to survival rates in patients treated with best supportive care; later, chemotherapy doublets consisting of third-generation agents in combination with platinum agents were shown to further improve 1-year survival rates, to 30% to 40%. Although chemotherapy causes side effects, symptoms are usually relieved and quality of life is usually improved in patients with advanced NSCLC treated with chemotherapy. In 5 phase III trials reported in 2000 and 2001, comparisons of several chemotherapy doublets comprised of a platinum paired with a third-generation agent showed that these regimens have quite similar im-
pacts on overall survival and quality of life. Thus, in selecting one regimen versus another, issues of toxicity, convenience of administration, and cost should be the dominant considerations. Third-generation agents improve survival, symptoms, and quality of life in patients 70 years of age or older as well as in younger patients. Two large randomized trials reported in 2000 showed that second-line therapy with docetaxel improves overall survival compared with survival after alternate chemotherapy (vinorelbine or ifosfamide) or best supportive care, establishing docetaxel as a standard in this setting. In the near future, some of the numerous biological therapeutics under preclinical and clinical study may be found to further extend survival and improve quality of life in patients with good performance status and may be shown to be reasonable treatment options for patients with poorer performance status.

**INTRODUCTION**

Lung cancer is the leading cause of cancer-related death in the United States and Europe. It is estimated that 169,500 people were newly diagnosed with and 157,000 people died of lung cancer in the United States in 2001 (Greenlee et al, 2000). Eighty percent of all cases of lung cancer are non–small cell lung cancer (NSCLC). Despite advances in the control of local disease, more people die from lung cancer than from breast cancer, prostate cancer, and colon cancer combined. This is in part because one third of patients with lung cancer present with metastatic disease. In addition, most patients treated with definitive therapy for local disease have a relapse, at which point they usually have disease that can no longer be eradicated. The focus of this chapter is systemic therapy for patients with clinically evident systemic disease either at presentation or at relapse.

**GOALS OF THERAPY**

Systemic therapy is the mainstay of treatment in patients with NSCLC with distant metastatic disease (stage IV disease) or malignant pleural effusion (stage IIIIB disease). Unfortunately, the 5-year survival rate with systemic therapy remains less than 5%. Until the 1990s, it was unclear whether there was a survival benefit from chemotherapy in patients with advanced disease. The natural history of metastatic NSCLC is grim, with a median survival time of about 5 to 6 months and a 1-year survival rate of 10%.

Meta-analyses published in the 1990s indicated that treatment with platinum-based regimens as opposed to best supportive care (BSC) in chemonaive patients increases lifespan about 6 weeks and doubles the 1-year survival rate to about 20% (Rapp et al, 1988; NSCLC Collaborative Group, 1995). In addition, despite the known risk of side effects of