Malignant pleural mesothelioma (MPM) is an aggressive, highly lethal neoplastic disorder of the pleural lining of the lung associated with exposure to asbestos. In the United States, about 2,000–3,000 new cases of MPM are diagnosed annually (Carbon et al., 2002). The prognosis is dismal, with a five-year overall survival rate of about 8% in the United States (Verschraegen, 2003).

Unfortunately, MPM generally presents at an advanced stage, and the prognosis is quite poor. Median survival is brief, about 6–18 months (Carbon et al., 2002). Available treatment options include surgery, radiotherapy, cytotoxic chemotherapy, and biotherapy. However, survival outcomes remain poor, and treatment is largely palliative and limited to supportive care. Because patients with MPM typically present at advanced age and have locally advanced disease and comorbid conditions, few are candidates for surgery. Although surgery can improve recurrence-free survival and provide palliative relief of pain and discomfort for patients with early-stage disease, less than 15% of these patients survive longer than five years (Vogelzang et al., 2003). Similarly, radiotherapy has been proven to be of limited value. Although radiotherapy is useful for the palliative treatment of painful metastases, curative radiotherapy is limited by the extent of tumor volume and potential toxicity to normal tissues (Scaglotti et al., 2003). Many cytotoxic agents, such as cisplatin, doxorubicin, and gemcitabine, have been studied as single agents and in combinations in phase II trials. Results to date with conventional agents have been disappointing. Response rates in single-agent studies typically range from 0%–15%. Median overall survival in most single-agent studies has ranged from seven to nine months. However, several studies have reported median overall survival rates from 5–11 months (Scaglotti et al., 2003).

Unsatisfactory results with conventional agents prompted increased research using newer agents with novel mechanisms of action. Perhaps the most significant new development in the treatment of MPM is the recent approval by the U.S. Food and Drug Administration (FDA) of pemetrexed (Alimta® [Eli Lilly and Company, Indianapolis, IN]), a novel multitargeted antifolate, in combination with cisplatin for front-line treatment of MPM.

Pemetrexed represents a significant advance in the treatment of MPM. Subsequent to demonstrating modest single-agent activity (response rate 14.1%; median overall survival 10.7 months) in a phase II trial of 64 patients with MPM (Scaglotti et al., 2003), pemetrexed, in combination with cisplatin, demonstrated significantly improved survival and...