Multiple myeloma (MM) is a B cell malignancy of the plasma cells. It is the second most common hematologic malignancy; only non-Hodgkin’s lymphoma is more common. About 14,600 cases of MM will be diagnosed in 2003, and approximately 10,900 people will die of the disease (Jemal et al., 2003). Recently published data on cancer incidence and mortality indicate a consistent decline in mortality rates for most cancers from 1991–1995. However, MM is one of three cancers that showed increased mortality rates for men and women, with increases of 5.6% and 3.6%, respectively (McKea-Cowdin, Feigelson, Ross, Pike, & Hender- son, 2000).

People affected by MM often are elderly, with a median age at diagnosis of 65 years. Eighty percent of patients are older than 60 years, and less than 3% are younger than 40 years. African Americans are affected by the disease twice as often as Caucasian Americans. MM is one of the leading causes of cancer death among African Americans (Blade, Kyle, & Greipp, 2002; Weber, 2002). The ef- fectiveness of treatment for MM varies widely, with remission rates for most cancers from 1970–2000. The mean survival rate with this regimen is about 72 months (Trippoli, Messori, Becagli, Alterini, & Tendi, 1998).

Clinical trials have tested numerous regimens to improve mean survival from time of diagnosis, but, until recently, none was found to be superior to melphalan and prednisone (Hjorth et al., 1999; Myeloma Trialists’ Collaborative Group, 1998).

Recent articles have reviewed the main therapeutic regimens for managing patients with MM (Campbell, 2002; Rajkumar, Gertz, Kyle, & Greipp, 2002; Weber, 2002). The ef- ficiency and safety of high-dose chemotherapy (HDC) and autologous stem cell transplantation is well established in myeloma and consi- dered standard therapy (Goldschmidt et al., 1997; Singhal et al., 2002). HDC has been used for more than 10 years as treatment for MM, ei- ther alone or with autologous hematopoietic stem cell rescue. It has improved remission, event-free survival, and overall survival rates in patients with MM (Attal & Harousseau, 1997; Harousseau & Attal, 1997).

At least one-third of patients with MM do not respond to induction chemotherapy, and those who initially achieve remission (even with HDC) eventually relapse and require additional treatment (Kyle, 1999). Because MM remains incurable and relapse is inevitable, a great need exists for novel therapeutic agents that can prolong life and improve overall survival rates for patients with MM.

### Immunomodulatory Drugs

Thalidomide (Thalomid®, Celgene Corporation, Warren, NJ), used empirically to treat MM based on its antiangiogenic activity and the increased angiogenesis observed in MM bone marrow, achieves re- sponses even in refractory, relapsed disease (Singhal et al., 1999). However, thalidomide has significant and dose-limiting side effects (Tariman, 2003), including somnolence, con- stipation, and neuropathy, which have prompted the search for more potent and less toxic thalidomide derivatives (Richardson, Schlossman, et al., 2002).

### Preclinical Studies

Immunomodulatory Drugs (IMiDs™) are potent thalidomide derivatives or analogs that markedly stimulate T cell proliferation, as well as...