Novel treatments of multiple myeloma

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Over the last decade significant advances in the treatment of multiple myeloma (MM) have been achieved. Most prospective randomized trials indicate that high dose therapy with autologous stem cell transplantation is associated with improved event-free and overall survival. Thalidomide, an oral immunomodulatory and anti-angiogenetic agent is associated with objective responses in 30% of patients with advanced and refractory MM. The addition of dexamethasone to thalidomide is associated with a 50% response rate in refractory patients and with a 70% response rate in previously untreated patients. This oral combination is particularly useful in newly diagnosed patients with features of advanced disease who are candidates for stem cell collection. Bortezomib is a potent and selective inhibitor of the 26S proteasome. Bortezomib has shown activity in 30% of patients with refractory/refractory MM including patients who have failed thalidomide. The combination of bortezomib with thalidomide and dexamethasone in previously untreated patients has been associated with a response rate exceeding 80%. More recently the Imid lenalidomide combined with dexamethasone has been associated with significantly higher response rates and longer event-free survival than dexamethasone alone. Lenalidomide and dexamethasone is also very active in previously untreated patients. The development of genomics and proteomics provide the basis for a novel molecular classification of MM, can identify unique targets for combination therapy in individual patients and provide the framework for clinical protocols to enhance cytotoxicity and to avoid the emergence of drug resistance.