The recent progress of bortezomib treatment for patients with multiple myeloma

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Advances in the understanding of the molecular pathophysiology of multiple myeloma (MM) and the mechanisms of drug resistance have led to dramatic changes in MM disease management in recent years and to the creation of new standards of care. Bortezomib, approved by the FDA in 2003 for the treatment of MM, has been a vital inclusion in the oncologist's armamentarium. A first-in-class, potent, selective and reversible small molecule inhibitor of the proteasome, bortezomib is highly active in the relapsed/refractory setting and is currently indicated for the treatment of MM at first relapse and in combination with melphalan and prednisone (MP) for front-line patients ineligible for transplantation, as evidenced by the VISTA trial. Recurring relapse is commonly associated with MM and several retrospective and prospective studies have highlighted the feasibility of retreatment with bortezomib, shown to evoke objective responses with no cumulative toxicity. The ongoing Phase II RETRIEVE study aims to further investigate bortezomib retreatment in patients who have previously responded to bortezomib. In those patients ineligible for transplantation, bortezomib plus MP was significantly superior to MP in terms of time to tumour progression, complete remission, objective response rate (ORR) and overall survival, including in those with high-risk disease. One-third of patients in the VISTA trial were aged more than 75 years and had similar efficacy results to those seen in younger patients. In effect, this showed factors traditionally associated with high-risk disease, such as age, may no longer be considered poor prognostic factors with the use of novel agents.

Bortezomib is also under investigation as an induction agent and studies have demonstrated its potential in this setting in combination with various treatment regimens, such as thalidomide plus dexamethasone or doxorubicin plus dexamethasone in the front-line setting. Interim study analyses indicate a high ORR with bortezomib versus controls, together with complete response rates pre- and post-transplant, which provides a strong case for this agent as part of induction regimens in the treatment of newly diagnosed MM. In addition to direct anti-myeloma activity, preclinical and clinical evidence also suggests a positive effect of bortezomib on bone remodelling due to increased bone formation and reduced bone destruction.

Overall, bortezomib offers rapid and durable results with consistently high rates of complete response in the management of relapsed/refractory MM and in patients ineligible for transplant. Studies have shown that treatment of MM with bortezomib is relatively well tolerated causing manageable non-haematological and haematological toxicity. In particular, peripheral neuropathy, the primary dose-limiting toxicity, can be managed with dose or schedule modification, supportive care and other therapies. Emerging evidence combining bortezomib with established and novel agents in the front-line setting is showing more promise than previous standards of care.

References


