# Bortezomib and restoration of chemosensitivity

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I read with great interest the Case Study by Chim and colleagues (Restoration of chemosensitivity by bortezomib: implications for refractory myeloma. *Nat. Rev. Clin. Oncol.* 6, 237–240)[1] in which they describe a 59-year-old woman with IgA multiple myeloma who relapsed after autologous bone marrow transplantation (ABMT), which was associated with paraprotein and an extramedullary localization to the pancreas head.[1] The authors stated that bortezomib added to cyclophosphamide, melphalan and prednisone (Vel–CMP) was able to restore chemosensitivity in this patient who was previously treated and was refractory to the same agents.

I would like to make a few comments and share some experience. It is true that the median time to response to bortezomib therapy is rapid and occurs within two cycles of therapy; however, some patients may take longer to respond. In total, 63 of the 256 (25%) patients in the SUMMIT and CREST trials were treated in an extension trial of SUMMIT (17 and 46, respectively).[2] Patients received a median of seven additional cycles of therapy, yielding a total median duration of therapy of 45 weeks or 14 cycles (median range 7–32 cycles). The results showed that patients who did not achieve a response could benefit from receiving eight or more cycles of bortezomib. In the case study reported by Chim and coauthors, it might be possible that the patient responded to bortezomib therapy alone instead of demonstrating chemosensitivity to alkylator agents.

In our center, we have treated 13 patients with relapsed/refractory multiple myeloma who have extramedullary localization of the tumor. A bolus injection of bortezomib (1.3 mg/m$^2$) was given on days 1, 4, 8 and 11 every 3 weeks. Pegylated liposomal doxorubicin was given intravenously at a dose of 30 mg/m$^2$ on day 4 every 3 weeks; 40 mg desamethasone was given intravenously on days 1–4 every 3 weeks, until a plateau phase was reached. At the time of bortezomib treatment, eight patients had disease relapse after ABMT.

Five patients who relapsed were previously refractory to anthracycline-based therapy such as vincristine, doxorubicin and dexamethasone (VAD). In total, 8 of 13 patients responded, and of these 5 had a complete response and 3 had a very good partial response. Moreover, 4 of the patients with disease refractory to VAD responded to bortezomib. Median response was reached after 1.5 months of therapy, but two patients needed six cycles of therapy. Finally, it would have been useful for Chim *et al.*[1] to have assessed the multidrug resistance status of these plasma cells before and after bortezomib treatment, because a reduction of this parameter could easily justify chemosensitivity.

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**Competing interests**
The author declares no competing interests.

1. Chim, C. S., Hwang, Y. Y., Pang, C. & Shek, T. W. Restoration of chemosensitivity by bortezomib: implications for refractory myeloma. *Nat. Rev. Clin. Oncol.* **6**, 237–240 (2009).
2. Berensen, J. R. *et al.* Safety of prolonged therapy with bortezomib in relapsed or refractory multiple myeloma. *Cancer* **104**, 2141–2148 (2005).