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approach for the treatment of multiple myeloma. However, a major problem associated with bortezomib treatment is the induction of cytotoxicity and apoptosis in non-myeloma cells. We investigated whether this is related to activation of the death receptors and consequent activation of the extrinsic apoptotic pathway. A cell-based model of myeloma and stromal cells was established to examine the impact of bortezomib on the myeloma cell death. The caspase inhibitor Z-VAD-fmk and poly(ADP-ribose) polymerase (PARP) inhibitor 3-aminobenzamide (3AB) were used to examine the effect of these inhibitors on apoptosis. The expression of the death receptors (DR) 4, 5 and 6 was quantified using qPCR and flow cytometry. In both the myeloma cell line and stromal cells, bortezomib induced apoptosis as

evidenced by propidium iodide staining, detection of hypodiploid cells by flow cytometry and activation of caspase-3 and PARP. Inhibition of caspases and PARP protected both the myeloma cell line and stromal cells from bortezomib-induced apoptosis. Bortezomib induced DR5 and DR6 mRNA expression in the myeloma cell line, but had no effect on mRNA levels in stromal cells. However, DR4 and DR6 were significantly induced in both cell types at the protein level. In addition, b 04aeff104c

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