tiation none of the patients had peripheral neuropathy > grade 1. Patients were scheduled to receive bortezomib 1.3 mg/m$^2$ IV (days 1, 4, 8 and 11) every three weeks for eight cycles and dexamethasone was planned to be added at a dose of 20 mg every other day (days 2, 5, 9, 12), if no signs of response were observed after the 1st cycle. Actually, 27 patients received dexamethasone and the 2 patients with plasma cell leukemia received thalidomide in addition. *Results*. Two patients in terminal resistant disease died prematurely and 3 patients are still receiving the 2nd cycle (thus, 5 patients are not evaluable at present). Overall, 39 out of 47 evaluable patients responded (83%) (3 complete remission [CR], 5 near CR, 25 partial response, 6 minimal response). The median time to response was 42 days. Within a median follow-up of 8 months (2-160), 16 (34%) patients relapsed and 8 patients (15%) died, 7 of disease and 1 of unrelated cause. In the majority of patients, non-neurologic toxicity was mild and reversible including fever, fatigue, gastrointestinal symptoms and hematologic toxicity. The most severe side effect was peripheral neuropathy which developed in 60% of patients. Neuropathy included ataxia, caustic pain and sensory disturbances and resolved after a median time of two months after discontinuation of Bortezomib. In most patients, treatment was reduced or stopped because of peripheral neuropathy but all responding patients completed at least 4 cycles. *Conclusion*. Bortezomib therapy alone or in combination with low dose dexamethasone produces rapid responses in relapsed and refractory MM. Early relapses are frequent. Neuropathy is the most important adverse reaction and lead to dose reduction or discontinuation of treatment.

## 0772

### BORTEZOMIB AS A SINGLE AGENT IN REFRACTORY/RELAPSED MULTIPLE MYELOMA RESULTS OF CZECH MYELOMA GROUP (CMG)

I.S. Spicka

*General Fac. Hosp. Prague, Prague, Czech Republic*

*Summary*. The efficacy of single agent bortezomib in the treatment of refractory multiple myeloma has been shown repeatedly. We summarize the results of bortezomib therapy in Czech republic. 82 patients with a median age 61 years (33-84) with refractory/relapsed myeloma were scheduled to receive Velcade 1.3 mg/m$^2$, on days 1,4, 8 and 11 mostly of a 21-day cycle. This was a heavily pretreated population (1-8 prior therapies, median 2), including high-dose therapy with stem cells support (56 patients, 68%) and/or thalidomide (42 pts, 51%). The overall results, assigned by EIBMT criteria, were as follows: the response was achieved in 40 patients (48.8%) - eight patients had complete (9%), 19 partial (29%) and 8 minor (9%) response. In 10 cases stabilization of disease was observed, 20 patients progressed during therapy, 5 died early after the start of therapy and in 7 cases the evaluation was not available due to short time of therapy. The response was observed early after the start of therapy in most cases, in 33 patients after the first cycle (40%) and in 11 after the second cycle (13%), although in minority of them progression during further therapy was observed. The most common adverse events were thrombocytopenia (65,9%) and neuropathy (52,4%), however, grade 3/4 thrombocytopenia developed in 37,8% and neuropathy only in 7,3% of patients, respectively. Other grade 3/4 complications were anemia (6%), granulocytopenia (13%), gastrointestinal events (8,5%), renal failure (6%) and infections (5%). *Conclusion*. Our experience confirmed that bortezomib provides clinical benefit with manageable toxicities in this heavily pretreated and high-risk population.

## 0773

### SYNERGISTIC GROWTH INHIBITION OF MALIGNANT PLASMA CELLS BY DEXAMETHASONE AND THE FARNESYLTRANSFERASE INHIBITOR L744.832

A. Ott, F. Bakker, K. Richter, T. Ahrens, R. Burger, A. Guenther, M. Gramatzki

2*nd Medical Department, Kiel, Germany*

*Background/Aim*. In this study, we assessed the in vitro efficacy of combinations of conventional and novel drugs on human multiple myeloma cell lines. Aim of this study was to test whether novel agents are able to enhance the response of malignant plasma cells towards conventional therapeutics. This may provide rationale for combination therapies which could improve the outcome of multiple myeloma. *Methods*. Cell lines JK-6L and L363 were incubated with various concentrations of drugs, alone or in combination, in the presence or absence of human bone marrow stromal cells (BMSC). Cell growth was measured in an MTS assay and results were evaluated for synergism. *Results*. It was found that dexamethasone (Dex) and the farnesyltransferase inhibitor L744.832 (L744) inhibited the growth of both cell lines in a synergistic fashion (e.g. 0.4 μM Dex reduced the growth of JK-6L cells to 91% of that observed in untreated controls, 0.4 μM L744 reduced growth to 38% of untreated controls, combining both agents reduced growth to 24%). Interestingly, L744 was able to restore Dex sensitivity of Dex resistant cells (JK-6L in the presence or absence of BMSC, L363 in the presence of BMSC) as well as to further enhance the sensitivity of Dex sensitive cells (L363 in the absence of BMSC). Furthermore, the rate of apoptosis, upon treatment of the cells with either agent alone or in combination, was determined by Annexin V (AxV) staining. Combining both agents enhanced the cytoxicity of either drug alone (e.g. in JK-6L cells, 0.1 μM Dex led to a 4.8% increase in apoptotic rate compared to untreated controls, 0.25 μM L744 led to a 10.7% increase, combining both agents led to a 21.4% increase), confirming the data obtained from the cell growth assays. *Summary/conclusions*. L744 synergizes with Dex and is able to enhance and restore the Dex sensitivity of malignant plasma cell lines. This in vitro study provides rationale to explore the use of this combination of agents in patients with multiple myeloma.