

The PAD (Ireland) study for patients with refractory and relapsed myeloma – an update.

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Introduction: The combination of Bortezomib with Adriamycin/Dexamethasone (PAD) is a highly effective induction agent with response rates of up to 95% (Oakervee et al, BJH 2005; 129: 755-62). We postulated that the superior efficacy of PAD chemotherapy could be demonstrated by studying patients who have been previously treated with VAD or a VAD-like regimen (VAMP, C-VAMP, Z-DEX etc.) by comparing the response to PAD given following relapse to the response previously obtained with the VAD or VAD-like regimen.

Materials and Methods: A Phase II study was developed with three cohorts, each planned to recruit 23 patients. Cohort 1; patients treated with VAD or VAD-like regimen who previously had an autologous transplant; Cohort 2 – similar patients but without previous transplant and Cohort 3 – patients refractory to VAD. Patients in groups 1 and 2 were allowed to have received one further line of treatment following VAD but patients in group 3 would proceed directly to PAD.

Results: Cohort 1 has been fully recruited. 8 patients achieved CR following PAD compared to 3 post-VAD $p=0.013$ using McNemar's Chi-squared test with continuity correction. Comparison of the fall in paraprotein showed a median fall of 89% post-PAD compared to 60% post-VAD, ($p<0.003$) Wilcoxon Matched Pairs Rank Test. There were no reports of increased cardiotoxicity. A number of patients proceeded on to second transplant following their response to PAD therapy.

6 patients have been recruited to group 2 and responses appear similar to patients in group 1. 18 patients have been recruited to group 3. In these patients, refractory to VAD-type chemotherapy nine of twelve currently evaluable patients have shown superior responses compared to a VAD-type chemotherapy. These results will be updated to include all currently enrolled patients and presented in detail.

Conclusion: PAD is a highly active therapy for patients with relapsed or refractory myeloma. The study provides supportive evidence for the use of PAD re-induction prior to second autologous transplantation currently being investigated in a randomised controlled clinical trial (NCRI UK) Myeloma X.