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Poster Session

Myeloma: Relapsed and Refractory Multiple Myeloma

Myeloma - Therapy, excluding Transplantation

PAD Given at Relapse Is More Effective Than VAD Given as Induction Therapy - Results of a Phase II Study.

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Abstract

Introduction: The combination of Vincristine, Adriamycin and Dexamethasone (VAD) followed by autologous transplantation has been a standard of care for patients with Myeloma for a number of years. Recently, it has been shown that a 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, in terms of both relative and absolute changes in the paraprotein or light chains and the degree of remission obtained by the standard EBMT criteria.

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**. A total of 42 patients have been recruited and as recruitment to cohort 1 is now complete, this report will focus on these 23 patients.

Results: 23 patients in Cohort 1 (9 females, 14 males) had a median age of 60 years (range 41–73). 8 patients had received thalidomide-based regimens following relapse after transplantation and had relapsed again. 15 patients were in first relapse. The time from diagnosis to **PAD** chemotherapy was 46 months (18–179 months). Previous

treatment given was VAD 13, C-VAMP 5, C-VAD 3, Z-DEX 2. Patients received a median of four cycles of **PAD**. 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. This difference was significant by the Wilcoxon Matched Pairs Rank Test (p<0.003). There were no reports of increased cardiotoxicity. A number of patients proceeded on to second transplant following their response to **PAD** therapy.

Conclusion: **PAD** is a highly active therapy for patients with myeloma in relapse, even if they have received a prior VAD or VAD-like regimen the differences are statistically significant despite the fact the patients have all experienced at least one relapse. **PAD** therapy will be incorporated into the NCRI (UK) Myeloma X regimen as an induction therapy in patients who have relapsed post autologous transplantation, with patients randomised to consolidation with a second autologous transplant or conventional dose cyclophosphamide.

Footnotes

Disclosure: Research Funding: Study funded by Jansen-Cilag UK through the All-Ireland Cooperative Oncology Research Group (ICORG). **Honoraria Information:** TCM has received Honoraria from Jansen-Cilag as a speaker (less than US $10,000). **Off Label Use:** Information is provided on the combination of Bortezomib with Adriamycin and Dexamethasone.