Phase I/II study of tandem high-dose chemotherapy with autologous peripheral blood stem cell transplantation for multiple myeloma

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[Objective] To investigate the safety and efficacy of tandem high-dose chemotherapy with tandem autologous peripheral blood stem cell transplantation (APBSCT) for treatment of advanced multiple myeloma.
[Patients and methods] Patient eligibility included confirmed diagnosis of stage II/III untreated multiple myeloma and patient ages between 15-64. The eligible patients were consequtively enrolled to the protocol and received 2-4 courses of VAD regimen. Those with progressive disease after VAD therapy were excluded. The responding patients underwent PBSC harvest following high dose cyclophosphamide and filgrastim. The first APBSCT following high dose melphalan (100mg/m^2 for 2 days) was performed within 2 months of PBSC harvest. 3-6months later, the second APBSCT was scheduled. The primary endpoints were feasibility, safety including treatment-related toxicity and protocol completion. The secondary endpoints were response rate, overall survival and progression-free survival.
[Results] Forty patients entered the protocol. A male: female ratio was 5:3. Their median age was 55(42-64). Sixteen of 40 patients had a stage II disease, and 24 of them a stage III disease. Immunoglobulin classes of M protein were IgG in 23 patients, IgA in 9, IgD in 1, Bence-Jones in 6, and non-secretory type in 1. Of these patients, 32 underwent the first APBSCT and 28 did the second APBSCT; the completion rate of the protocol was 70%. Treatment-related mortality was 2.5% (n=1) throughout the protocol. Severe toxicity (non-hematologic grade 4 toxicity) occurred in 12.5% and 14.3% in the first and the second APBSCT, respectively. All but one who died achieved hematopoietic recovery, suggesting the feasibility and safety of the protocol. Among 28 patients who completed the second APBSCT, the results were favorable with a response rate of 65% (complete response rate 27.5%, n=11); 3-year overall survival was 89%, and 3-year progression-free survival 34% at a median follow-up of 562 days.
[Conclusion]Tandem high-dose chemotherapy with APBSCT is feasible and safe with favorable response rates in the treatment of advanced multiple myeloma. These observations suggest that this combined modality may be further investigated.